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JULY
1957

VOL LVIII
NO VII

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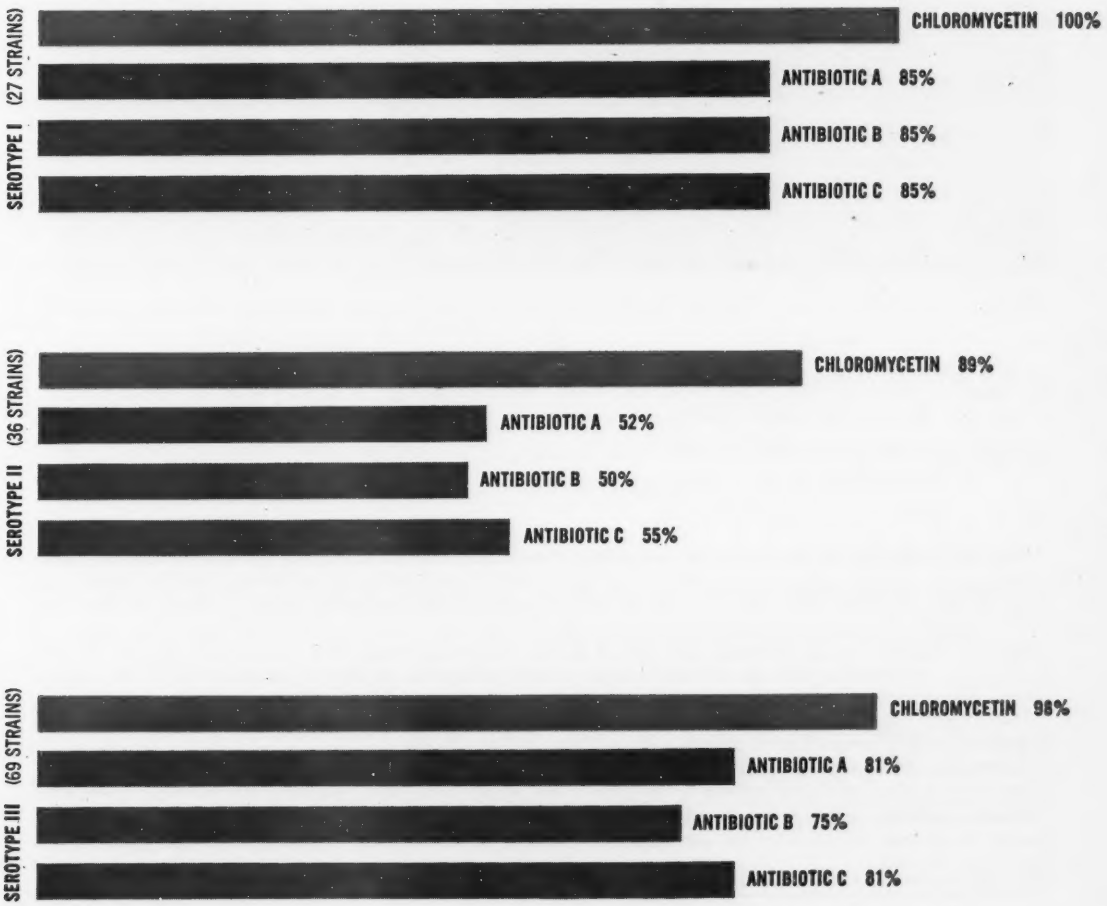

*This graph is adapted from Metzger & Jenkins.[1]
Inhibitory concentrations were 12.5 mcg. or less.

THE JOURNAL
of the
KANSAS MEDICAL SOCIETY

Volume LVIII JULY, 1957 Number 7

TABLE OF CONTENTS

Original Articles

Lung Cancer—A Problem Emphasized by Increasing Frequency of this Lesion—Martin J. FitzPatrick, M.D., Kansas City 433

Gastric Acidity—Study of Neutralizing Effects of Antacids and Discussion of Titrimetric vs. Electrometric Determinations—Paul J. Uhlig, Kansas City, and Henry N. Tihen, M.D., Wichita 437

Abdominal Trauma—Rupture of the Jejunum and Hemopneumothorax following Non-Penetrating Trauma—Evan R. Williams, M.D., Dodge City 446

Colorado Tick Fever—Observations on Eighteen Cases and Review of the Literature—Curtis C. Drevets, M.D., Iowa City . . 448

Editorials

Whither, When, and Why 457

How the Other Half Lives 461

Leading Causes of Death 461

Miscellaneous

President's Page 456

Clinicopathological Conference—Vomiting, Anemia, Confusion, and Convulsions . . 463

Choline—A Review of Indications for Therapeutic Use—Robert G. Godfrey, Kansas City —Thesis 474

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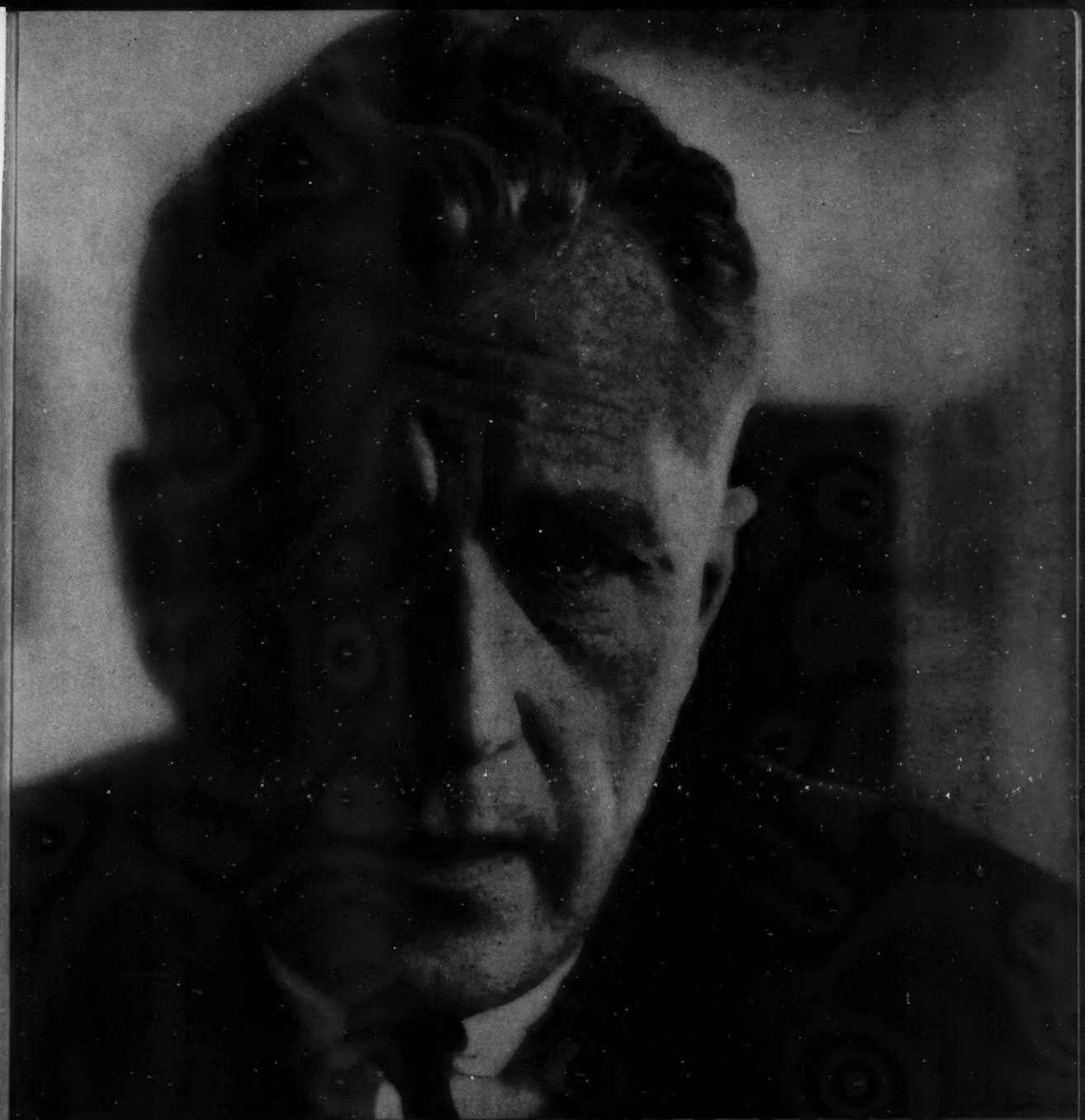

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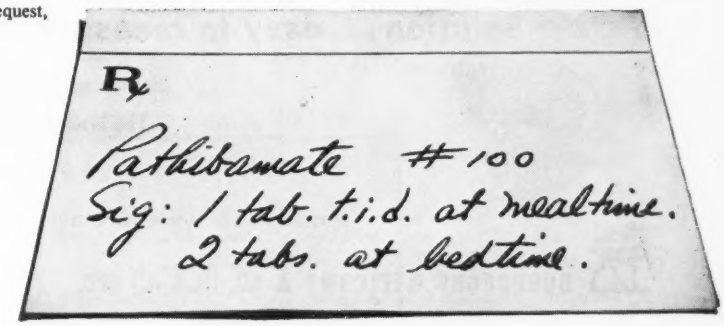

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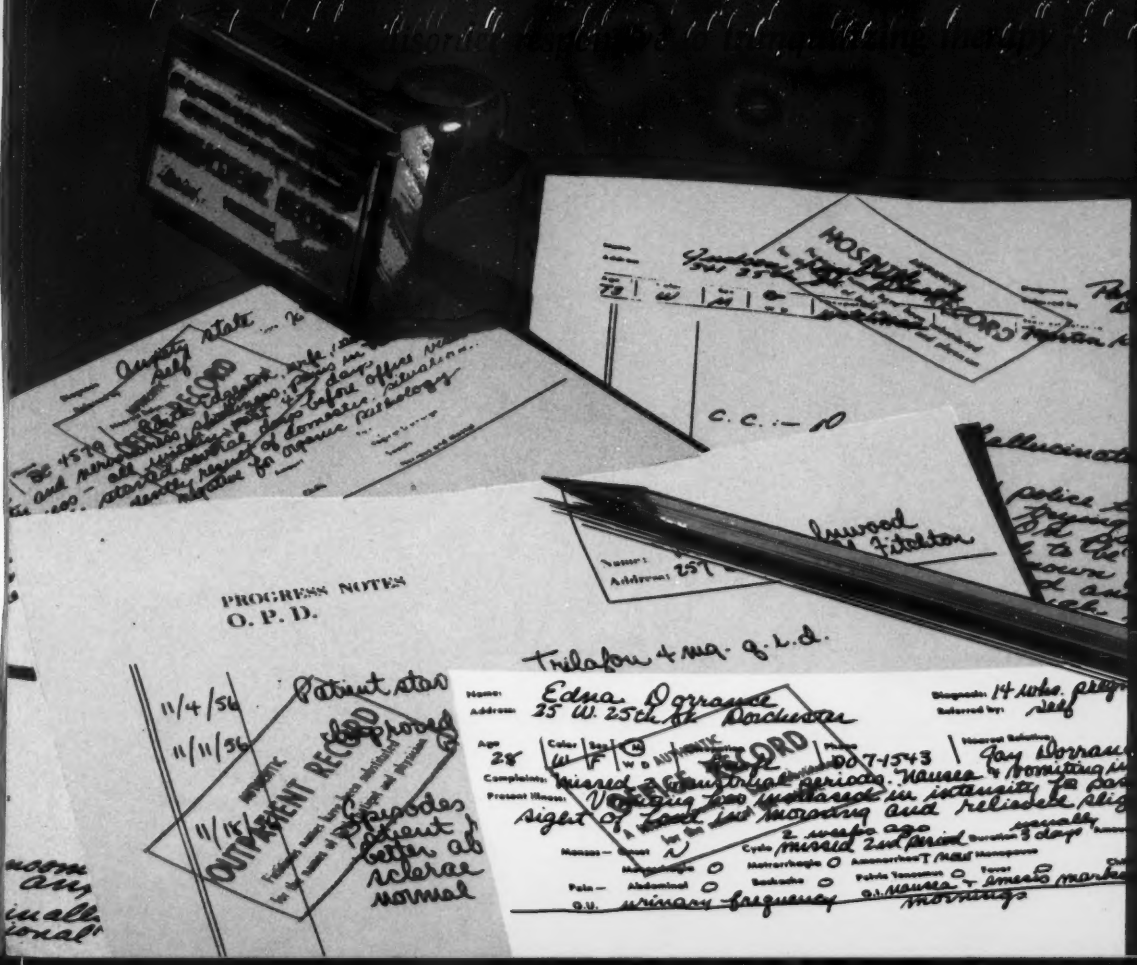

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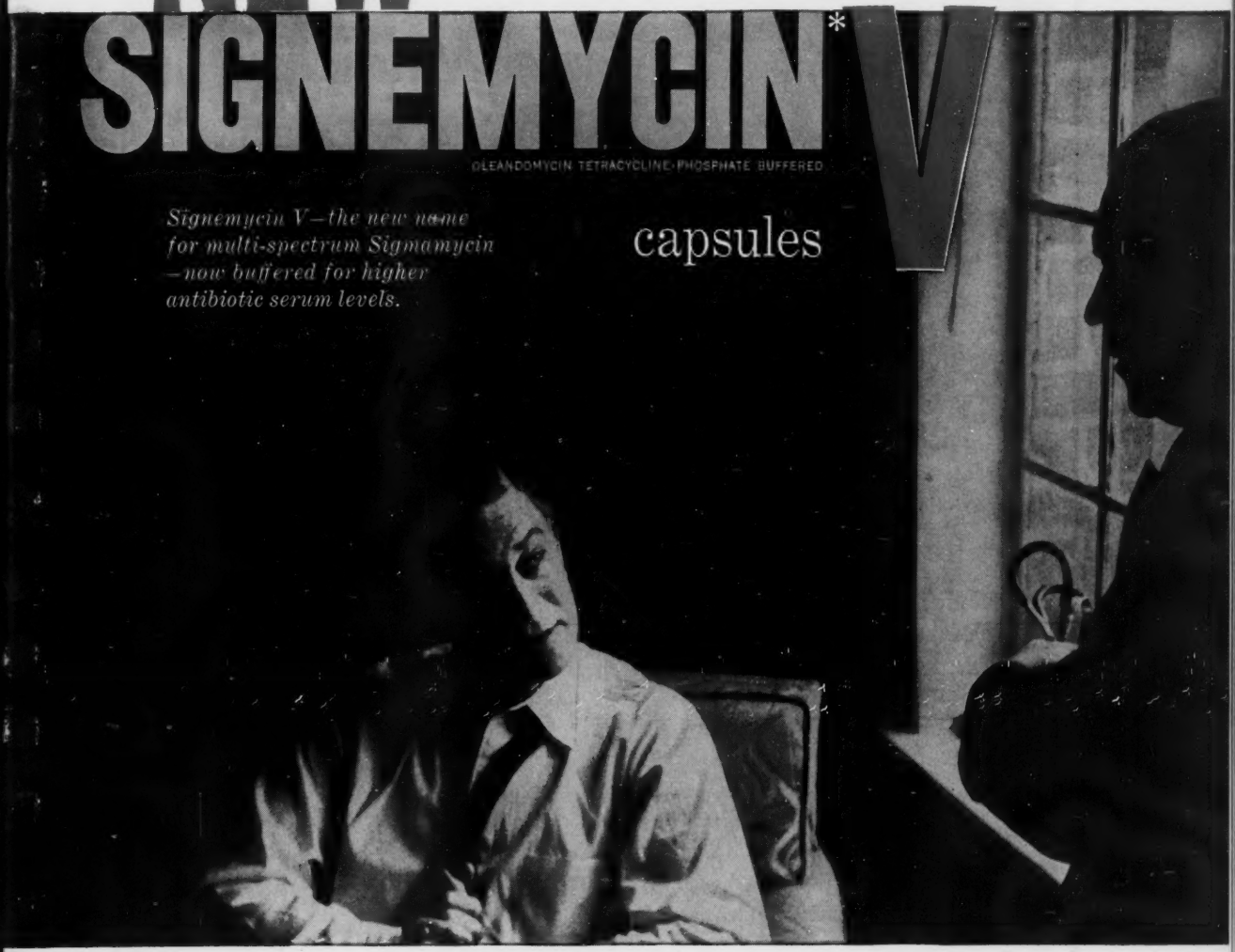

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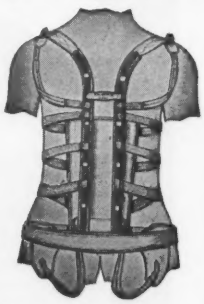

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Volume LVIII **JULY, 1957** **No. 7**

Lung Cancer

A Problem Emphasized by Increasing Frequency of This Lesion

MARTIN J. FITZPATRICK, M.D., ***Kansas City***

The second quarter of the 20th century has been marked by an increasing medical awareness of the growing problem of primary lung cancer. Since 1930, mortality from these tumors has increased 500 per cent, and in many communities primary bronchogenic carcinoma has become the commonest malignant tumor of the adult male.[1] We are all aware of a changing epidemiological knowledge concerning pulmonary carcinogenesis, with the gradual removal of this entity from the domain of a pure occupational disease and its evolution into an every-day problem for the practicing physician.

Ever since the 16th century description by Paracelsus of the "mala metallorum" of the Schneeberg miners of Saxony, man has been vaguely aware of lung cancer associated with mining.[2] It was later established that radioactivity in these mines was the contributing factor, a fact further documented recently in the uranium mines of Joachimstal, now behind the Iron Curtain.[3] Down through the years an increased occupational toll of lung cancer has been noted in radium laboratory workers, in nickel refineries, and in chromate workers, among others.[4,5]

Of the 27,000 Americans who died of lung cancer in 1955, few were employed in these industries, and epidemiologists for many years have been seeking other explanations. To date it has been strongly suggested that increasing industrial atmospheric pollution, growing use of carcinogenic petroleum derivatives, and the four-fold rise in the cigarette smoking habits of our civilization are probably all likely contributors to the steadily rising tide of pulmonary carcinogenesis.[6,7] The growing statistical evidence linking excessive cigarette smoking with some forms of bronchogenic carcinoma has been further augmented by recent careful pathologic examinations of the respiratory system.[8] These studies have shown an additional significant association between excessive smoking and pre-cancerous lesions of the lung.[9] While future studies will be required to prove many of these complex problems, knowledge of their existence, however, does offer today's citizens, including physicians, an opportunity to practice some form of preventive measures.

The seven-year experience at this hospital with some 400 patients with lung cancer has been reviewed. There were seven surgical patients living at least five years after diagnosis. Factors contributing to a successful outcome have been noted.

In considering our present treatment of lung cancer, the picture across the nation remains a gloomy one. Our best method of treatment, surgical extirpation of the lesion, often appears to be only a palliative tool and is at best available to about one-third of the lung cancer population.[10] Despite the pursual of an aggressive surgical attack on this problem in the 20 years that followed the first successful pneumonectomy for lung cancer, patient survival has not improved. For despite the striking growth in skill of the thoracic surgical attack in this period of time, there has been no appreciable improvement in finding patients earlier in the course of their disease.

Turning to this community, an analysis of a seven-

From the Section for Pulmonary Disease, Department of Medicine, University of Kansas Medical Center. Presented in part at the Postgraduate Pulmonary Disease Clinic, January 14, 1957.

CANCER OF LUNG
K. U. M. C.
1948-1955

Total Patients	428	
Male	360	(84%)
Female	68	
Dead	391 (91%)	Five Year Survival 7 (1.7%)
Treatment		
None	187	(44% of total)
Surgery	126	(29% of total)
Palliative	45①	
"Curative"	81	(64% of those operated; 19% of total)
X-Irradiation	97②③	(25% of total)
Nitrogen Mustard	15	(3.5% of total)
Others	3	

①Combined with X-Irradiation 7
②Combined with Nitrogen Mustard 10

Figure 1. Patient survival and types of treatment given.

year experience with primary lung cancer at the University of Kansas Medical Center has been made. Some of the statistics used in this study have been obtained from the tumor register maintained at this hospital since 1948. Other data were obtained from study of hospital charts and records, including roentgenograms. When possible, five-year survivors with lung cancer have been interviewed and studied from the point of view of recurrence of tumor. When this was not possible, the personal physician of the survivor was contacted and asked to report on the patient. In addition, commoner male tumors were also studied during this same period of time for comparative purposes. Since the bulk of these patients were referred by practicing physicians from the state of Kansas, it should prove of interest to attempt an analysis of some factors responsible for a successful outcome in the few five-year survivors.

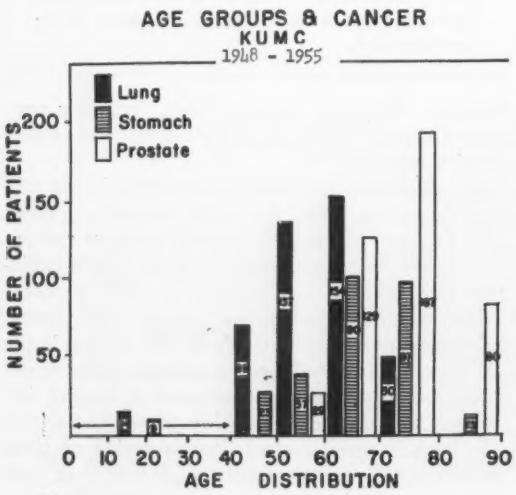

Figure 2. Age grouping of three male cancers.

Results

In the seven years between 1948 and 1955, 428 patients were diagnosed as having primary lung tumors. As seen in Figure 1, a large number were deemed inoperable, and a definitive surgical attack was made on only 19 per cent of all patients. Of those patients operated on, roughly two-thirds were considered to be "curative" procedures. Of these, seven have survived at least five years. There were no comparable non-surgical survivors, and 91 per cent of all patients were dead when this analysis was made.

Figure 2 shows the age distribution between three commoner male tumors studied in this group of patients. In this series carcinoma of the lung generally appeared earlier than the other tumors, with prostatic malignancies being seen in an older group of males. This fact should be emphasized in considering survival from these different tumors, for the attrition from cardiovascular and infectious diseases should be greater in the older population. Figure 3 points out the differing therapeutic implications of these tumors, as well as the remarkable difference in survival of male patients with cancer of the prostate. This striking difference points out the importance of true therapeutic and palliative agents available in the management of hormonally dependent male tumors. However, many of these prostatic malignancies were diagnosed histologically, without clinical evidence of invasion at the start of treatment.

COMPARATIVE MALE CANCERS
KUMC
1948-1955

	Lung	Stomach	Prostate
Total Patients	360	181	431
% Receiving "No Treatment"	44%	33%	6%
Alive at Time of Study (Patients)	31	22	152
5 Year Survivals (Patients)	6	6	76

Figure 3. Results of treatment of male cancers.

The seven known five-year surgical survivors are described in Figure 4. It should be noted that most of these patients had symptoms of relatively short duration preceding thoracotomy. All of the males had a central, obstructing, well differentiated squamous-cell tumor, only half of which could be identified through the bronchoscope. In two males, the can-

Clinical Data on Surgical "Cures"
KUMC
1948-1955

Patient Age at Operation Race, Sex	Duration of Symptoms	Occupation	Bronchoscopic Biopsy	Surgical Procedure	Tumor Classification	Regional Lymph Node Metastases	Known Survival
1 GM,43yr,W ♂	1 Month	Warehouse Foreman	0	Left Pneumonectomy	Squamous Cell Ca	+	7 Years
2 FN,57yr,W ♀	5 Months	Housewife	0	Rt Lower Lobectomy	Anaplastic Ca	0	8 Years
3 CT,60yr,W ♂	3 Months	Farmer	+	Rt Pneumonectomy	Squamous Cell Ca	0	9 Years
4 JL,60yr,W ♂	6 Months	Farmer	+	Rt Pneumonectomy	Squamous Cell Ca	0	5 Years
5 HG,60yr,W ♂	2 Months	Farmer	0	Rt Upper Lobectomy	Squamous Cell Ca	0	7 Years
6 DB,64yr,W ♂	3 Months	Clerk	+	Left Pneumonectomy	Squamous Cell Ca	0	5 Years
7 CC,65yr,W ♂	4 Months	Farmer	0	Rt Pneumonectomy	Squamous Cell Ca	+	8 Years

Figure 4. Clinical data on surgical survivors.

cer had metastasized regionally beyond the lung at the time of operation, despite which both patients are still living and free of tumor. These two individuals stress the often overlooked fact that the first successful pneumonectomy for lung cancer, done in 1933 by Dr. Evarts Graham on a fellow-physician, was for this same type of tumor.[11] In that instance regional metastasis outside of the lung had already occurred, despite which the physician was able to pursue a full 20 years of practice following operation.[12] It should also be pointed out that five of the seven survivors were age 60 or over at the time of operation, and that four have lived at least five years with only one lung. Thus age, in itself, should not be considered a contraindication to the required surgical procedure for removal of the malignancy.

A few of the survivors will be considered in greater detail to illustrate some important aspects of their clinical story. Mrs. F. N. was a 57-year-old housewife when first seen in 1949 with a five months' history of chronic cough and hemoptysis for two months. Chest roentgenograms (Figure 5) disclosed a mass in the right lower hilum, which on lateral view is seen in the superior segment of the lower lobe, overlying the 7th dorsal vertebral body. On study she was found to have a negative tuberculin skin test, a normal bronchoscopy, and no acid-fast bacilli on sputum smear. A right lower lobectomy

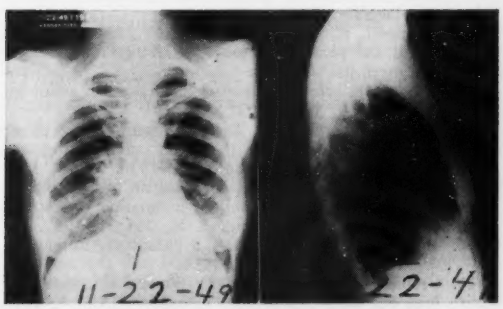

Figure 5. Preoperative roentgenograms on F. N. showing a right lower lobe mass.

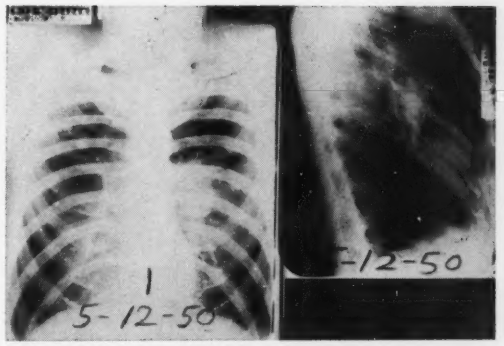

Figure 6. Preoperative roentgenograms on C. M. showing a left hilar mass.

was performed in 1949 for a necrotic, peripheral, anaplastic carcinoma. No tumor was found in lymph nodes removed with the specimen. This patient is living and well today without further treatment, free of evidence of tumor despite the limited resection for this poorly differentiated peripheral carcinoma. This is certainly an unusually fortunate result, far from the expected prognosis of this early metastasizing tumor.

Mr. C. M. was a 43-year-old foreman, referred in 1950 with a one month's history of persistent cough, associated with a mass in the left hilum shown in Figure 6. On study he was found to have a normal bronchoscopy, and laminograms (Figure 7) suggested a malignant tumor about the left upper lobe bronchus. He was found to have a tumor arising from the left upper lobe. A left pneumonectomy was carried out, and the specimen disclosed a well-differentiated squamous cell carcinoma, with metastatic tumor in the carinal and peribronchial lymph nodes. The patient had no further treatment and is living

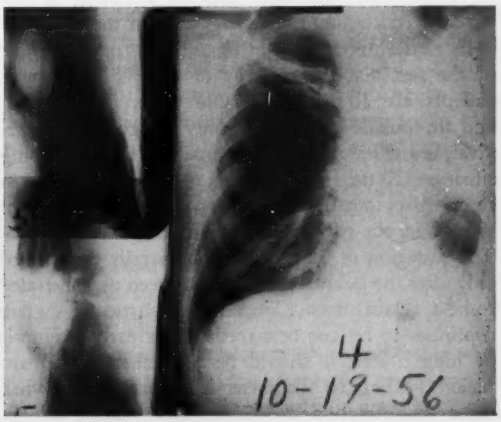

Figure 7. Preoperative laminograms of left hilar mass. Postoperative appearance of chest six years later.

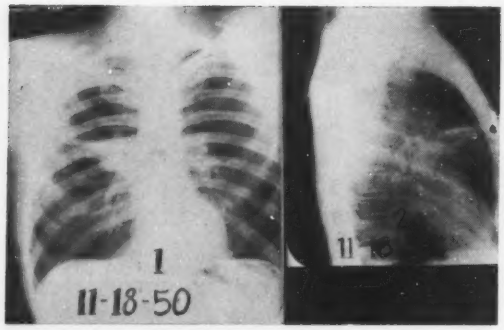

Figure 8. Preoperative roentgenograms on H. G., showing obstructing right hilar mass.

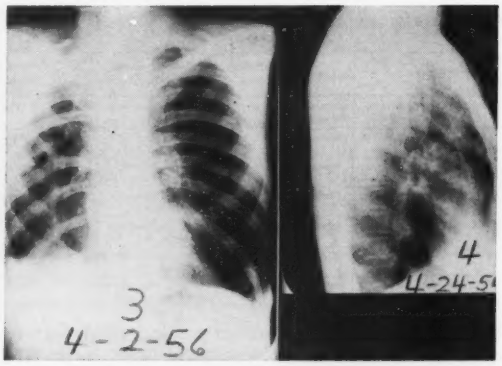

Figure 9. Postoperative roentgenograms on H. G. six years after lobectomy.

and well today, without evidence of recurrence of cancer.

The last representative patient, H. G., was a 60-year-old farmer referred in 1950 with a two months' history of chronic cough, weight loss, and a persistent abnormality of the right lung on repeated chest roentgenography, similar to that seen in Figure 8. Work-up included a normal bronchoscopy, and the patient subsequently was explored. He was found to have a tumor of the right upper lobe which was resected by a right upper lobectomy. The specimen contained a squamous-cell carcinoma, with no tumor found in the lymph nodes removed. This man had no further treatment and is living and well today without evidence of recurrence of cancer. Figure 9 shows postoperative chest roentgenograms no different from more recent ones. This patient demonstrates that a local resection of a malignant tumor of this type, in the absence of known metastases, can be followed by a six-year survival. This strongly suggests that other factors, at present unknown, governing rates of cell multiplication and invasion or spread of tumors may eventually call for a change in our thinking concerning the management of these lesions.

In analyzing this group of patients, one is struck by the fact that the majority of today's lung cancer patients are already inoperable when first studied, and are thus deprived of the only real chance for survival and cure. A principal cause for this disturbing situation is the lack of any real improvement in recent years in early detection of potential lung cancer victims in our patients or in the general population. The suspicion of lung cancer is generally entertained only after the pulmonary lesion has been demonstrated to be a persistent one. Since the chest roentgenogram continues to be our best method for early diagnosis of lung cancer, it should be remembered that suspicion leading to diagnosis is possible only when some manifestation of the invasive nature of the tumor has shown itself—thus, it is already a fairly advanced lesion. It is hoped that during the next seven-year period a practical clinical test for biological activity of early tumors will be forthcoming, which will allow us to use our surgical tools to their greatest advantage. Beyond that, it can be hoped that other studies will eventually offer a practical method for prevention of most of today's pulmonary malignancies.

Acknowledgement

The author would like to express deep appreciation to all physicians who assisted in following these patients and acknowledges generous help given by members of the Departments of Pathology and Surgery in preparation of this report.

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Gastric Acidity

Study of Neutralizing Effects of Antacids and Discussion of Titrimetric vs. Electrometric Determinations

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PART I. A STUDY OF THE NEUTRALIZING EFFECTS IN THE HUMAN STOMACH OF COMMONLY USED ANTACIDS

There is as yet much to learn about the neutralizing effects of antacids in the human stomach as commonly used in the treatment of peptic ulcer. Two methods of study of this problem are at present available, namely, the recording of pH readings from an indwelling gastric electrode and, secondly, the study of acidity changes in aspirated gastric contents.

The recording of readings from an indwelling gastric electrode has been long in the process of development and is a method of much promise. However, it still awaits the development of an easily usable gastric electrode which must have the following qualifications to make its use easy and accurate. To permit long continued studies comfortably, it must be small enough for nasal introduction. It must be of suitable flexibility and suitably weighted at the distal end, so that it will always be accurately positioned by gravity when introduced into the stomach. This latter point is an important consideration, since the positioning of the tube in different parts of the stomach must be accurately controllable in order to obtain comparable readings. Third, from previous studies[1, 3] it seems desirable that the small glass electrode bulb be sheathed in some type of fenestrated covering that will prevent it from lying directly in contact with the gastric mucosa, while allowing free flow of gastric contents over the bulb.

Since such an electrode is not completely worked out at this time, this study has utilized the method of aspirating small amounts of gastric contents at 15-minute intervals and the determination of the neutralizing effects of various antacids by titration of these specimens.

There are numerous reports of the theoretical and in vitro neutralizing values of various antacids, but they are given in terms of various standards, such as 0.1 N HCl, 0.143 N HCl, 0.17 N HCl, 0.3 per cent HCl, 0.5 per cent HCl, etc. It would be desirable to use some single standard unit for these reports, and the natural one would seem to be milligrams or milliequivalents of HCl neutralized by a given amount of antacid, perhaps one gram.

Johnson and Duncan[8] have devised a suitable method for testing the in vitro neutralizing power of various antacids measuring the amount of neutralization obtained in 10 minutes at 37 degrees Centigrade with stirring. This method may well be used for in vitro testing, and the use of the 10-minute reading is important, since in vivo the stomach is rather quickly emptying out any given antacid, and to be effective in vivo an antacid must neutralize quickly. The use of a 10-minute neutralization reading is a helpful means of judging the clinical value of an antacid. The neutralizing power of various antacids in vitro thus determined by Johnson and Duncan expressed in cc. of 0.1 N HCl and in milligrams of HCl neutralized is shown in Table I.

In Part I the relative neutralizing power of the commonly used antacids is evaluated. In Part II the difference between free acid readings determined electrometrically and those determined titrimetrically is emphasized.

Kraemer[8] found the relative in vitro neutralizing values of antacids to be as follows, expressed in relationship to sodium bicarbonate as 100 per cent:

Magnesium oxide	372%
Calcium carbonate	177%
Sodium bicarbonate	100%
Magnesium trisilicate	100%
Tribasic calcium phosphate	31%
Aluminum hydroxide gel	13%

The theoretical neutralizing power and the in vitro neutralizing power of various antacids give some indication of their probable effects in vivo. However, when it is realized that in the maximum hypersecretion in ulcer patients perhaps about 12,000 mgm. of HCl are produced in 24 hours, and that in the

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Since completion of this paper the first named author has received his M.D. degree from the University of Kansas School of Medicine and is now serving his internship at Camp Pendleton Naval Hospital, Camp Pendleton, California.

TABLE I

Antacid	*Amount of Antacid*	*Cc. of 0.1 N HCl Neutralized in 10 Minutes*	*Mgm. of HCl* Neutralized in 10 Minutes*
Magnesium oxide	1 gram	432	1576
Aluminum hydroxide gel	16.7 grams of 6% gel	280	1022
Calcium carbonate	1 gram	175	638
Aluminum hydroxide powder	1 gram	130	474
Sodium bicarbonate	1 gram	118	429
Magnesium trisilicate	1 gram	92	335
Aluminum trisilicate	1 gram	36	131

* 1 cc. of 0.1 N HCl contains 3.65 mgm. of HCl
Vol. of HCl in cc. x normality = milliequivalents of HCl in that volume
Vol. of HCl in cc. x normality x 36.5 = milligrams of HCl in that volume

average duodenal ulcer patient around 5,000 mgm. of HCl are produced each 24 hours, and that this latter amount would be completely neutralized by 8 grams of calcium carbonate, it becomes evident that the in vitro neutralizing effects of the antacids are greatly reduced in the stomach, and their actual effects can be determined only by in vivo studies. The effect of an antacid in the stomach is greatly modified by the constant emptying process of the stomach, the rate of reaction of the antacid, and perhaps by little understood diffusion processes in the stomach wall between the gastric contents and the blood plasma.

Sippy[9, 10] and Palmer and Kirsner[11, 12] and others have done much work evaluating the in vivo effects of antacids in ulcer patients. On the basis of in vivo studies, Kirsner and Palmer[11] rate the various antacids as follows in decreasing order of neutralizing effects:

1. Calcium carbonate 4.0 grams
2. Calcium carbonate 2.0 grams
3. Heavy powders—Calcium carbonate 2 grams, and sodium bicarbonate 2 grams
4. Aluminum hydroxide 30 cc.
5. Intermediate powders—Calcium carbonate 1.2 grams, and sodium bicarbonate 2 grams
6. Tricalsate 4.0 grams
7. Tribasic calcium phosphate 4.0 grams
8. Aluminum hydroxide 16 cc.
9. Simple powders (Sippy No. 1)—Calcium carbonate 0.6 gram, and sodium bicarbonate 2.0 grams
10. Sodium bicarbonate 4.0 grams
11. Aluminum hydroxide 4 cc.
12. Magnesium trisilicate 1.0 gram

The above evaluation was obtained on the basis of hourly aspirations over an entire day. In our study we have desired to see what information could be gained from more frequent aspirations at 15-minute intervals after administration of a number of the antacids in clinical use and in clinically usable dosages. The theoretical 10-minute neutralizing power, based on Johnson and Duncan's values in Table I of each

TABLE II

Antacid	*Amount of Antacid*	*Theoretical Neutralizing Power* IN CC. OF 0.1 N HCL	IN MGM. OF HCL
No. II Sippy tablet	Sodium bicarbonate 10 grains Magnesium oxide 10 grains	365	1332
No. I Sippy tablet	Sodium bicarbonate 30 grains Calcium carbonate 10 grains	353	1288
Calcium carbonate	30 grains	350	1277
Amphojel	30 grains	260	949
Sodium bicarbonate	30 grains	236	861
Gelusil	35 grains	236	861
Liquid Gelusil	12 cc.	236	861
Robalate	30 grains		

of the antacids in the amounts used in this experiment, is shown in Table II.

Method of Study

All studies were made on one trained subject, a normal, healthy male, 27 years of age. Fifty-one experiments, each of five hours' duration, were carried on nearly daily over a period of three months. The same standard breakfast consisting of orange juice, oatmeal with milk and cream, buttered toast, and coffee was ingested each morning at 8:00 o'clock. At 8:30 a.m. a Levine tube, size 14F, was introduced through the nose to a distance of 26 inches. The Levine tube was of such weight and flexibility that in this subject at this distance the end of the tube went immediately into the pyloric portion of the stomach and remained there. It was checked fluoroscopically, daily at first and later every two or three days. On every x-ray check the end of the tube was found positioned in the pyloric antrum. This is important as in different subjects and with different weights and flexibilities of the Levine tube, the end of the tube may take various positions in the stomach. The tube was maintained in situ for the duration of each daily experiment.

Aspirations of 5 cc. of gastric contents were begun at 9:00 a.m. and carried out at 15-minute intervals until 1:00 p.m. The antacid was given with 100 cc. of distilled water each hour, at 9:00 a.m., 10:00 a.m., 11:00 a.m., and 12 noon, immediately after the removal of the 5 cc. aspiration sample on the hour. Except for the liquid Gelusil, the antacids were given in tablet form, the tablets being crushed a few times by the teeth and washed down with 100 cc. of water. The following determinations were made on each specimen using a Beckman pH meter for the pH readings and standard 0.1 N NaOH solution:

1. pH of the aspirated specimen
2. Titration of free acid with 0.1 N NaOH to end point of pH 3.5
3. Further titration with 0.1 N NaOH to bring specimen to color change with phenolphthalein indicator for total acidity

After a control day for each series, the antacids were used in order on consecutive testing days. It was planned to have a total of five series of determinations on each antacid. However, due to time limitations of the subject, only four series of determinations were made on liquid Gelusil and Robalate, and three series on milk and cream, calcium carbonate with milk and cream, and Amphojel with milk and cream. It would seem desirable in general to use a minimum of five experiments even when using the same subject, to prevent errors from the daily fluctuations that occur in gastric secretions. However, the general pattern of reaction to each antacid was fairly uniform throughout, and it would seem, in an experiment of this nature with a trained subject, that five repetitions of each series give an accurate picture.

In an experiment of this kind, there is not space to present all of the readings taken, but the results may be portrayed in two ways as presented in Table III. In this table the average of all of the 15-minute readings in clinical units of free acid for the same period of time is given, and likewise the number of readings without any free acid is also given. Each of these methods reveals the relative neutralizing effects of the different antacids.

In Table III the lettered columns represent the following experiments:

Column A: Control Series—100 cc. distilled water at 9-10-11-12

Column B: Milk and cream—100 cc. milk and cream at 9-10-11-12

Column C: Sodium bicarbonate—grains 30 with 100 cc. distilled water at 9-10-11-12

Column D: Sippy No. 2—1 tablet (sodium bicarbonate grains 10 and magnesium oxide grains 10) with 100 cc. distilled water at 9-10-11-12

Column E: Calcium carbonate—3 tablets (grains 30) with 100 cc. distilled water at 9-10-11-12

Column F: Calcium carbonate—3 tablets (grains 30) with 100 cc. milk and cream at 9-10-11-12

Column G: Amphojel—3 tablets (grains 30) with 100 cc. distilled water at 9-10-11-12

Column H: Amphojel—3 tablets (grains 30) with 100 cc. milk and cream at 9-10-11-12

Column I: Sippy No. 1—1 tablet (sodium bicarbonate grains 30 and calcium carbonate grains 10) with 100 cc. distilled water at 9-10-11-12

Column J: Robalate—4 tablets (grains 30) with 100 cc. distilled water at 9-10-11-12

Column K: Gelusil—3 tablets (grains 35) with 100 cc. distilled water at 9-10-11-12

Column L: Liquid Gelusil—12 cc. with 100 cc. distilled water at 9-10-11-12

Discussion

The degree to which the acidity of the gastric contents should be reduced to permit healing of peptic ulcers is not known.[13] Some assume that it should be reduced to the so-called proteolytic end point of pH 4.5 to 5, at which pepsin is no longer active. More believe that if the free acid is abolished, which occurs at pH 3.5, healing occurs. There is clinical evidence that healing certainly occurs when the acidity is not reduced to this point. However, it would seem desirable to reduce the acidity to the point of no free acid insofar as it is possible to do so.

TABLE III

TIME	Control A	Milk and Cream B	Sodium Bicarbonate C	Sippy II D	Calcium Carbonate E	Calcium Carbonate With Milk & Cream F	Amphojel G	Amphojel with Milk & Cream H	Sippy I I	Robalate J	Gelusil K	Liquid Gelusil L
9:15	23	21	15	4	4	9	9	5	0	0	12	5
9:30	24	27	12	3	3	2	8	11	0	0	17	10
9:45	30	28	11	8	0	6	15	18	5	11	21	16
10:00	37	30	14	11	5	11	35	14	17	16	19	17
10:15	46	27	30	0	0	0	20	9	0	12	3	18
10:30	35	33	15	4	4	0	9	10	5	12	16	29
10:45	40	38	12	5	3	0	21	16	18	21	32	30
11:00	41	50	38	22	8	0	17	26	29	39	30	35
11:15	27	25	19	3	0	0	11	21	22	4	17	16
11:30	30	17	22	0	0	0	5	30	44	18	10	20
11:45	23	35	26	3	8	0	13	36	38	20	17	27
12:00	33	49	25	12	34	0	22	39	37	21	15	47
12:15	31	34	2	3	0	0	9	5	3	7	17	16
12:30	39	22	0	9	11	0	12	4	9	10	15	39
12:45	44	31	17	22	13	0	15	25	30	28	20	42
1:00	51	46	11	25	30	0	8	27	58	7	39	43
Average free HCl	34	33	17	8	8	2	14	18	20	14	19	26
Total No. of 15-minute readings	75	48	70	78	74	46	75	47	73	53	71	60
No. of readings no free acid	1	0	30	50	45	39	22	10	33	20	12	6
% of times of no free acid	1	0	43	64	61	85	29	22	45	38	17	10

The testing of 15-minute aspiration samples reveals how difficult it is to attain complete neutralization with antacids alone, due largely to the constant emptying of the stomach which tends to rather quickly pass the antacids out of the stomach and thus greatly decrease their neutralizing effects.

The persistence of considerable free acid in these experiments on the hourly administration of antacids in a normal subject makes it clear that continuous neutralization of free acid by antacids alone will usually not be obtained in hypersecreting ulcer cases and certainly dictates that the amount of antacids administered should not be less than those used in this study. Based on the amount of the average reduction of free acid determined by the titration of the 15-minute samples, the neutralizing value of the antacids used would be in the following order of descending value:

		Clinical Units
No. II Sippy—1 tablet	average free acid	8
Calcium carbonate—3 tablets (grains 30)	" " "	8
Amphojel—3 tablets (grains 30)	" " "	14
Robalate—4 tablets (grains 30)	" " "	14
Sodium bicarbonate—3 tablets (grains 30)	" " "	17
Gelusil—3 tablets (grains 35)	" " "	19
No. I Sippy—1 tablet	" " "	20
Liquid Gelusil—12 cc.	" " "	26
Milk and cream—100 cc.	" " "	33
Control	" " "	34

Arranged in order of neutralizing value as determined by the percentage of the 15-minute aspirations showing no free acid, the antacids would be in the following order of descending value:

No. II Sippy	No	free	acid	readings	64%
Calcium carbonate ...	"	"	"	"	61%
No. I Sippy	"	"	"	"	45%
Sodium bicarbonate ...	"	"	"	"	43%
Robalate	"	"	"	"	38%
Amphojel	"	"	"	"	29%
Gelusil	"	"	"	"	17%
Liquid Gelusil	"	"	"	"	10%
Milk and cream	"	"	"	"	0%
Control	"	"	"	"	1%

In Column F of Table IV, an interesting experience is shown, namely, that when the same amount of calcium carbonate is given with half and half, instead of with water, its neutralizing effects were markedly increased in a set of three daily experiments. However, when Amphojel was given with half and half, instead of with water, its neutralizing effects were not increased. This result needs further study to prove or disprove these findings.

Conclusions

1. On the basis of testing of 15-minute aspiration samples of gastric contents, the relative neutralizing power of the commonly used antacids was evaluated.

2. The difficulty and improbability of complete neutralization of free acid by antacids alone given intermittently are demonstrated. This is undoubtedly due to the rapid elimination of the antacids from the stomach while more hydrochloric acid is being formed.

3. Certainly smaller amounts of antacids than those used in this study would be of relatively little neutralizing value.

4. The use of milk and cream with calcium carbonate greatly increased the neutralizing effects of the calcium carbonate.

5. Hourly feedings of milk and cream alone do not lower gastric acidity.

6. The use of one antacid (Gelusil) in liquid form did not give as good neutralization as the same antacid in tablet form.

PART II. TITRIMETRIC VERSUS ELECTROMETRIC DETERMINATIONS OF FREE HYDROCHLORIC ACID IN GASTRIC ANALYSIS

One of the most commonly used measurements in the study of gastric contents is that of free acidity determined titrimetrically with the use of 0.1 N NaOH to a color end point with Topfer's reagent or to an electrometric end point of pH 3.5 through the use of a pH meter. A second method of measuring the acidity of gastric contents is the measurement of the pH of the gastric content either intragastrically through an indwelling gastric electrode or on aspirated specimens which may be mathematically transferred into degrees of free hydrochloric acid. In this study on relative neutralizing power of various commonly used antacids, an opportunity has been presented to compare the pH readings on over 700 aspirated gastric specimens with the titrimetrically determined free acid readings on these same specimens, thus giving an opportunity to compare and evaluate the two methods.

Method of Study

The method of study important to this part of the report is that under standardized conditions on the same trained subject, 15-minute aspirations of 5 cc. of gastric contents were done from 9:00 a.m. to 1:00 p.m. daily with various test antacids being given each hour with water or milk and cream, and also a control series with water alone and with milk and cream alone on the hour. The determinations on each specimen were made immediately after aspiration by the same individual (P.J.U.) through the entire series so as to insure uniform technical results. The following readings were made on each specimen using a Beckman pH meter for the pH readings and standard 0.1 N NaOH solution:

1. pH of the aspirated specimen
2. Titration of free acid with 0.1 N NaOH to end point of pH 3.5
3. Further titration with 0.1 N NaOH to bring specimen to color change with phenolphthalein indicator for total acidity

For the purpose of this part of the report, only the above readings of No. 1 and No. 2 are used, consisting of the pH of the aspirated specimen and the clinical units of free acid as determined by titrating to an end point of pH 3.5. A graphic presentation of these readings is presented in Table IV.

For reference and for the sake of clarity, Table V is given to show the different modes of expressing gastric acidity.

Discussion

The findings in Table IV conclusively demonstrate that pH readings on gastric contents and titrimetric free acidity readings do not measure the same thing and cannot be transferred back and forth as equivalent readings. It is noted that practically without exception the titrimetric free acid readings are higher than free acid readings deter-

TABLE IV

FREE ACID IN CLINICAL UNITS AS DETERMINED BY TITRATION

Free Acid in Clinical Units as Calculated from pH Reading	48	38	30	23	18	14	10	8	6	5	4	3	2	2	2	1	1	1	1	1	1	0	0
pH Readings	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0	3.1	3.2	3.3	3.4	3.5	3.6 to 7.0
5 Control Days	40	78	72	45	29	38	32	30	18	26	26	12	48						3			0	No Free Acid Readings
	60	33	24	42	41	36	36	19	21	11		14											
		29	33	52	65	46	32																
		44	29	59	18	34	24																
		41		49	24	32	17																
		43		36	29	36	14																
				38	23	31	20																
				34	44	14																	
				28	28	14																	None
				23	31	37																	
				27	26	39																	
				35	25	26																	
				47		27																	
				29		23																	
5 Days Sodium Bicarbonate		57	37	35	42	27	20	17	20	20		20		10	6			2	3				00000000
		51	47	42	29	29	22		12			21		8	11				3				00000000
		50	32	29	32	51	22					9											00000000
		47	33			26						17											000000
		41				34																	
						19																	
5 Days Calcium Carbonate	51	57		24	24	43	22	19	11	17	12	13	4	11		6		5				0	00000000
					18	16		36			15	6	21			13						0	00000000
						17		39			8	14										0	00000000
								11			14											0	00000000
																						0	00000000
5 Days Gelusil Tablets			58	41		56	23	25	31	41	16	13	21		11	15	7	8		2		0	00000000
				36		33	26	26	21	29	18	14	9				15	11		2			000
				42		37	32	39	17	19	28	9	12										
						36		31	20	23		17	9										
						25		20	17	14		12	15										
								17	19	14		11											
								22	17			16											
								25	19														
									17														

TABLE IV (Cont.)

pH Readings	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0	3.1	3.2	3.3	3.4	3.5	3.6 to 7.0
Free Acid in Clinical Units as Determined by Titration	42	26 45 51 57 51	45 57 44 32 40 37	34 49 42 48 57 29	54 16 31 31	29 25	45 17	29 8 17 18 20	19	20 22 14	12	38 17	17 16	12 10	9		13 7	10 6	6 4		4	0	No Free Acid Readings 00000
4 Days Liquid Gelusil				43 34 33 35																			
5 Days Sippy I	42	57 50 62 42 41 34 39 43	53 52 34 25 42 54	47 43 34	25 37 20 31 37	25 24	31 19 27	16		11 23 14	11 11	10				11	5 9					0	00000000 00000000 00000000 00000000
5 Days Amphojel				37	51 25 30	29 22 38	30	25 17 16 16 20 26 21	25 34 22	23 20 10 20 15 16	13 24	48 17 6 30 6 17 11 10	11 12 18 14	36 7 7 34 11 21	47 21	10 5	8	12	8	4	2	0 0 0 0 0	00000000 00000000 0
5 Days Sippy II	43 13	61 31	39 57		39 18 27 24	19	19 16 7 24	19 20 21	17 19 17 23		11 13 10		23		17		15						00000000 00000000 00000000 00000000 00000000 00000000 00

TABLE IV (Cont.)

pH Readings	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0	3.1	3.2	3.3	3.4	3.5	3.6 to 7.0
Free Acid in Clinical Units as Determined by Titration				45 52			22 39 30 29	27	23	14	33 26	21 27 22	34	34 12	21 20 29	7 9 20 14 15	6 17 9	11 14	4	7	0 0	0 0 0 0 0	No Free Acid Readings 00000000 0000
4 Days Robalate																						0	
3 Days Milk & Cream	44 57	51 42	38 54 41	33 27 29 28 31 30	34 33	26 27 23 22 21 31 24 27	30 34 36 24 31 27 21	25 27 22 16 22 26 21	28	30 20	14	22						4					None
3 Days Calcium Carbonate and Milk & Cream									22			14	11			12				7 4		0 0	00000000 00000000 00000000 00000000 000000
3 Days Amphojel and Milk & Cream			45	41			28 39	37	20 37 37 28 32	27 19 22	16 15 20	30 32 15 16	11 14	15 21 12	12 12 20	11 16 17	9 8 9		5			0 0 0 0	000000

TABLE V

MODES OF EXPRESSING ACIDITY*

Clinical Units	*Milliequivalents Per Liter*	*Per Cent*	*Milligrams Per cc.*	*Normality*	*pH*
170	170	0.620	6.20	0.17	0.88
160	160	0.583	5.83	0.16	0.90
150	150	0.547	5.47	0.15	0.93
140	140	0.510	5.10	0.14	0.96
130	130	0.474	4.74	0.13	0.99
120	120	0.438	4.38	0.12	1.02
110	110	0.401	4.01	0.11	1.06
100	100	0.365	3.65	0.10	1.10
90	90	0.328	3.28	0.09	1.14
80	80	0.292	2.92	0.08	1.19
70	70	0.255	2.55	0.07	1.24
60	60	0.219	2.19	0.06	1.31
50	50	0.182	1.82	0.05	1.38
40	40	0.146	1.46	0.04	1.47
30	30	0.109	1.09	0.03	1.59
20	20	0.073	0.729	0.02	1.76
10	10	0.036	0.365	0.01	2.04
5	5	0.018	0.182	0.005	2.33
1	1	0.0036	0.036	0.001	3.01
0.1	0.1	0.00036	0.0036	0.0001	4.00

* By permission from *Peptic Ulcer* by Ivy, Grossman, and Bachrach. Copyright, 1950. Blakiston Division, McGraw-Hill Book Co., Inc.

mined by the pH reading. The meaning of this seems clear and does not detract from the value of each type of reading. The pH reading measures the free acid present at the moment of reading. The titrimetric free acid reading measures the amount of free acid present plus the additional amount of free acid liberated as hydrogen ion from a combined state, as titration is carried to the free acid end point of pH 3.5. In other words, the pH reading determines the actual free acid present. The titrimetric reading is that of the free acid actually present plus the potential amount of free acid that will be liberated if neutralization of gastric contents proceeds.

As an example, the free acidity as calculated for pH 1.9 would be 14 degrees. However, in Table IV for the first five control days, the free acidity readings by titration on the specimens showing a pH of 1.9 averaged 31 degrees. This same difference between the free acidity determined by the pH readings and the free acidity determined by titration is noted throughout all of the determinations.

Conclusions

1. The above study demonstrates and emphasizes the difference between the free acid readings determined electrometrically and titrimetrically, and demonstrates that they actually measure different things.

2. The pH readings measure the actual free acid present and the titrimetric readings measure the actual free acid present plus the potential free acid that might be liberated from its combined state.

3. Although the total acidity readings are not presented in this paper, it is noted in our measurements that the greater the total acidity as determined by the phenolphthalein indicator, the greater is the difference between the pH free acidity reading and the titrimetric free acidity reading.

4. Table IV graphically portrays the relative neutralizing value of the commonly used antacids on a trained subject under uniform conditions by the degree of the shift of the pH readings to the right and by the relative number of readings with no free acid.

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(Continued on Page 472)

Abdominal Trauma

Rupture of the Jejunum and Hemopneumothorax following Non-Penetrating Trauma

EVAN R. WILLIAMS, M.D., *Dodge City*

Periodic reports in the literature concerning rupture of the intestine from non-penetrating abdominal trauma make one cognizant that this entity must be considered in all cases seen in emergency states. The mortality rate is alarming if this condition is not recognized.

In 1935 Counseller and McCormack[1] reported on 1,313 cases with total mortality of 73.4 per cent. Poer and Woliver[8] in 1942 added 199 cases with a mortality of 61.2 per cent. Reports since then show a lower mortality with increased recognition and with more intensive management.

Perforation most commonly occurs in those areas of the intestine which are relatively fixed by mesenteric attachments, (1) duodenum, (2) jejunum near the ligament of Treitz, and (3) ileum just proximal to the ileocecum.

Case Report

This report is being presented to show an interesting traumatic case with several associated problems which arise from traumatic injuries seen in a small hospital.

A 20-year-old white male was brought to the emergency room by the police after having been thrown from a car in an accident in a small community near Dodge City. The exact circumstances surrounding the accident were unknown. He was found lying near a telephone pole, and it was presumed that he had been thrown and had struck his abdomen against it. He did not lose consciousness and was complaining only of severe pain over his appendiceal area when admitted. He felt that he had appendicitis.

Physical examination at that time revealed a 20-year-old white male in apparent shock. Blood pressure was 90/70. There was a small contusion over the left forehead. The right shoulder was deformed. The clavicle was separated from the acromion distally, and there was pain on motion of the shoulder. His respirations were labored. Both lung fields were initially clear to percussion and auscultation except for a diminution of breath sounds on the right side, but this was not marked. Examination of the head, ears, eyes, and throat was negative except for pallor of the mucous membranes. Pupils were equal in size and reacted to both light and accommodation. There was some bleeding from mucosal tears in the mouth.

The abdomen had no scars. It was muscular and not distended. Liver, kidneys, and spleen were not palpable. There was a diffused tenderness with rigidity over the entire left side of the abdomen with minimal tenderness on the right side. The bladder was distended but not tender. There was no pain on pressure over the chest wall or on compression of the chest or hips. There was marked pain on compression over the abdomen. Back, joints, and extremities were negative except for deformity of the right shoulder.

Perforation of a hollow viscus must be suspected when there is persistent abdominal pain, spasm, and tenderness subsequent to severe trauma to the abdomen, either with or without nausea or vomiting.

Radiographs revealed the chest to be clear. There were separations of the sternal junction of the first, second, and third ribs with a fracture in the midaxillary line on the third rib. There was a stellate fracture through the scapula itself.

During the course of the radiographs the man vomited approximately 2,000 cc. of thick food with no relief from pain. It was elected to explore him immediately. The preoperative diagnosis was (1) ruptured spleen and (2) rupture of a hollow viscus.

A small left rectus incision was made, and bleeding points were not clamped. The rectus fascia was split vertically, the muscle was separated, and the general peritoneal cavity was entered. A large amount of bluish blood presented itself shortly after the incision was opened. It was not welling up in the manner that one associates with a ruptured spleen, however. The incision was enlarged proximally and distally until the hand could be placed in the general peritoneal cavity. The spleen and liver felt normal but the stomach was dilated. A Cantor tube was passed into the stomach by the anesthetist. Intestines and stomach were then packed away medially and

distally until the spleen could be visualized, and there was no active bleeding. The small intestine was run for a distance of about one foot from the ligament of Treitz. Two holes were found in the jejunum, one measuring approximately 2 cm. across. The mucosa was everted. The holes were closed with intestinal suture in two layers with imbrication of the serosa over the holes. There was a tear in the mesentery of the jejunum, and this was closed on both sides. The examination of the rest of the ileum revealed no further injury. There was no Meckel's diverticulum.

Examinations of the liver, stomach, and gallbladder were normal. There was a large hematoma in the lesser omentum, and the entire lesser curvature of the stomach was surrounded by hematoma. The incision was closed without drains. The patient was given 1,000 cc. of whole blood and was returned to his room in a satisfactory condition.

The following morning he seemed to be in good condition. A catheter had been inserted into his bladder, and there were red and white cells in the urine specimen. These did not clear until his discharge from the hospital two weeks later.

On the first postoperative day his right chest filled with fluid, causing a loss of breath sounds from the right side and a definite lag of the chest on this side. A thoracentesis was done, and a No. 24 Robinson catheter was inserted in the chest cavity and placed in an underwater seal. About 500 cc. of liquid blood drained from the chest cavity. On the third day his chest was clear. He was passing gas. A repeat chest x-ray on September 4 revealed a pneumothorax still present. The hemothorax was gone. The lung was expanding. On September 5 the Cantor tube was clamped and the catheter was removed from his bladder; on September 6 the underwater seal was discontinued; on September 7 the Cantor tube was removed, and he began to eat. The sutures were removed on the tenth postoperative day. The patient was ambulatory. He was discharged to return to the Navy on the 15th postoperative day.

The final diagnosis was fracture of the ribs fourth in the anterior axilla line; separation of the first, second, and third ribs from their sternal junction; stellate fracture of the right scapula with dislocation of the clavicle from the scapula; right hemopneumothorax; perforated jejunum; contusion of kidney and bladder and hematoma of the mesentery.

This paper is presented to illustrate how, without any external evidence of severe injury, this man was critically ill from complications that can arise from both abdominal contusions and chest injuries. It illustrates once again the necessity for a complete history and physical examination and careful watching of the chest in all traumatic postoperative patients.

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We Americans live in a scientific world. We use scientific and technological developments to reduce backbreaking labor, to gain shorter working hours and higher pay, to raise our living standards to the world's highest. That is why the scientist's job concerns everybody vitally. Today's pioneer does not wear a coonskin cap or shoulder a rifle. More likely he is wearing a laboratory apron and wielding a stirring rod. He continually finds new lands to explore in his test tubes. His hunting is done with the microscope. He seeks new horizons in the cyclotron.

—*Robert E. Wilson*

Colorado Tick Fever

Observations on Eighteen Cases and Review of the Literature

CURTIS C. DREVETS, M.D., ***Iowa City, Iowa***

Colorado tick fever, apparently the only tick-transmitted viral disease of man in the western hemisphere, was one of the unknown fevers encountered by the first immigrants in the Rocky Mountain region. It is an acute, benign, non-exanthemic disease characterized by an intermittent fever, which only in the past few years has been clearly recognized as a distinct disease entity.

The author had the opportunity to study a series of 18 cases of Colorado tick fever during the summer of 1955 in the Estes Park Clinic, Estes Park, Colorado. The purpose of this paper is to present an informative summary emphasizing the clinical observations on these cases, together with a review of the pertinent literature to complete the study of the disease.

Historical Background

Colorado tick fever has been experienced by white man since he first immigrated to the Rocky Mountain region. Undoubtedly it existed among the American Indians before that time. Early physicians in the region had difficulty in differentiating this non-exanthemic disease from malaria and typhoid fever, and often it was considered a mild form of either disease. As early as 1855, Ewing[7] discussed "mountain fever" in the literature as an acute, benign, intermittent, non-exanthemic febrile disease. He reported a detailed account of the symptomatology, course, his treatment, and a proposal that the etiology was rarefied mountain air. Numerous reports[25,33] of this mountain fever, which may have been confused with other fevers, appeared in Army medical reports in the latter half of the 19th century.

About 1873 an exanthemic fever (Rocky Mountain spotted fever) was first described, and this proved to be much more serious. Scientific studies of these mountain fevers as a group began about 1880. For several decades the true mountain fever was confused with the spotted fever and was usually considered a mild form of the latter; earlier, the observers of both considered them separate diseases. During the first two decades of the 20th century, reports of mountain fever were overshadowed in the literature by the great interest in Rocky Mountain spotted fever. Not until 1926 did Becker reawaken some interest in the disease by suspecting the wood tick as the etiologic agent.

In 1930, Becker[1,2] accurately described the clinical picture and proposed the name of Colorado tick fever, which still stands today. The following year Toomey[29,30,31] wrote a number of articles on the same disease, still calling it American Mountain tick fever. Most of the work on Colorado tick fever has been done in the past 12 years at the University of Colorado Medical Center by Florio and his associates.

This study indicates that it is becoming increasingly important for doctors outside the endemic area of this disease to be able to diagnose Colorado tick fever since the areas of exposure are often frequented by tourists who can easily journey to their homes before the symptoms appear. This is especially important for physicians whose patients often vacation in tick-infested areas. Although the diagnosis of Colorado tick fever is not a life or death issue, it may save physicians embarrassment and further diagnostic studies.

Etiology

The etiology of Colorado tick fever remained unproved until 1944 when Florio[15,18] and associates experimentally transmitted the disease serially in humans and hamsters. They showed the causative agent to be a filterable virus transmitted by the bite of the wood tick, Dermacentor andersoni Stiles. The virus[13,20,21] readily passes Berkefeld N and W candles and single Seitz EK pads. Using graded collodion membranes, the hamster-adapted virus was estimated by Florio, Mugrage, and Stewart[13] in 1946 to have a diameter of ten millimicra. Koprowski and Cox[20,21] estimated the diameter to be from 35 to 50 millimicra. The virus is stable, surviving for at least three and one-half years on ice and readily preserved by

This paper was written while the author was a student at the University of Kansas School of Medicine. He has completed an internship at the Weld County General Hospital, Greeley, Colorado, and is now beginning a residency in internal medicine at the University of Iowa Hospitals.

TABLE I

AGE, SEX, HOME OF PATIENT, HISTORY OF EXPOSURE, AND INCUBATION PERIOD.

Case No.	*Patient*	*Sex*	*Age*	*Home State or Country*	*Tick Exposure*	*Days before Symptoms*
1	W.R.†	M	45	Colo.	bite	?
2	E.P.	M	56	Nebr.	bite	5-7 d.
3	J.D.	M	19	Iran	bite	2½ d.
4	F.S.	M	60	Nebr.	bite	1 d.
5	E.H.	M	17	Fla.	bite	5 d.
6	A.H.†	M	54	Ind.	body contact	?
7	A.Mi.	M	72	Nebr.	bite	3 d.
8	A.Me.	F	6	Ill.	bite	⊕
9	K.F.	M	9	Mo.	bite	2 d.
10	H.D.†	M	45	Ill.	body contact	2 d.
11	B.M.†	M	53	Nebr.	bite	2 d.
12	H.B.	M	16	Ill.	bite	2 d.
13	C.N.	F	18	Colo.	bite	3 d.
14	G.M.†	M	72	Kans.	bite	2 and 4 d.
15	J.Z.	M	24	Nebr.	bite	7 d.
16	F.K.	M	50	Fla.	bite	⊕
17	C.W.*	M	45	Colo.	bite	3 d.
18	H.J.*	F	43	Colo.	bite	1 d.

* Native to tick infested areas.
† Summer residents in tick infested areas for several years.
⊕ Tick first found at time of physical examination.

freezing or drying. It is inactivated at 60 degrees Centigrade for 30 minutes.

The virus has been successfully transmitted in the following laboratory animals: golden hamster, white mice, dilute brown agouti mice, and developing chick embryos.[17,19,21] Complement-fixation tests by DeBoer and associates[5] and neutralization tests carried out in mice by Koprowski and Cox[22] and others[9,26] have shown the Colorado tick fever virus to be different from the viruses of dengue, yellow fever, rabies, Russian spring-summer encephalitis, Venezuelan equine encephalitis, eastern and western equine encephalitis, Japanese B encephalitis, St. Louis encephalitis, lymphocytic chorio-meningitis, and louping-ill, as well as from the rickettsiae of Rocky Mountain spotted fever, murine typhus, and American Q fever.

Many experimental viral studies have been done in the past decade. Further discussion of the virus is beyond the scope of this paper, and the interested reader is referred to the literature cited above.

Pathology

Pathological findings in the human having Colorado tick fever are unknown. No authenticated deaths due to Colorado tick fever have been reported. Furthermore, there are no reports in the literature of autopsies being performed on persons having this disease and dying of other causes.

The only available information on pathology in this disease is from Black, Florio, and Stewart[3] in their study of the golden hamster infected by the virus of Colorado tick fever. Their findings are limited to the spleen of the hamster. The splenic reaction is definite on the second day of the illness, is most pronounced on the third day, and is progressively less intense on the fourth and fifth days. Although gross swelling of the spleen is not a prominent feature, the term acute splenic tumor was applied by the above investigators.

The main microscopic findings are alterations in the cellular types and the arrangement of the follicular lymphoid tissue. There is an apparent reduction in the number of lymphoid cells in the central portion of the follicle, with the appearance throughout the follicle of large pale-staining mononuclear cells mingled with polymorphonuclear leukocytes and erythrocytes. These large mononuclear cells contain small, irregularly shaped masses of dark blue-staining materials resembling fragmented nuclei. The periphery of the follicle shows a partial or complete disappearance of the well-defined margin, being replaced by a ragged border of mononuclear cells with occasional neutrophils or erythrocytes.

Also in the hamster the average leukocyte count is lowest on the fourth day, at which time cytoplasmic bodies are usually found in the lymphocytes. The

previously described splenic reactions are well correlated with the leukocyte count and the presence of these cytoplasmic bodies.

Clinical Study

During the summer of 1955, approximately 25 patients at the Estes Park Clinic were suspected of having Colorado tick fever. Eighteen of these were observed and studied as well as was possible on an out-patient basis. A number were transient vacationers who were somewhat difficult to follow. All except three of the 18 cases were observed between June 7, 1955, and July 10, 1955, the three exceptions being observed during the month of August. The first period corresponds with the height of the tick season in the area and the second period with a rainy season which brought the ticks out of hiding again.

Age and Incidence

As can be seen in Table I, the ages of the patients varied between 6 and 72 years; however, most were adults. All but three were males. Although this series is far from large enough to make any conclusions about the age and sex of the patients, it seemed to roughly correspond with the population which was being exposed to the tick habitats. This agrees with the reports of other investigators of the disease.[23] The true incidence of the disease in any locale is, of course, difficult to determine, especially in a resort area where the population is highly mobile and transient. Patients in this series represent approximately one in every 175 patients who entered the clinic. It is difficult to estimate the number of persons having Colorado tick fever who did not seek medical advice at this central clinic. This is further discussed in the following section.

Epidemiology

Becker[1,2] in 1930 suspected the wood tick as the transmitting agent of Colorado tick fever. In 1944, Florio and colleagues[17] attempted to infect humans with supposedly infected ticks but failed; however, they were able to transmit the disease serially in humans by parenteral injection of the blood or serum of infected humans. The same investigators[10] reported in 1948 the direct transmission of the disease from infected wood ticks to the golden hamster and in 1950[12] reported the isolation of the virus of Colorado tick fever from Dermacentor andersoni Stiles in nature. They also demonstrated the transovarial transmission of the virus in the wood tick.[12] In the same year these investigators[10,11] reported the isolation of the virus of Colorado tick fever from the dog tick, Dermacentor variabilis, found on Long Island, New York.

The wood tick has an interesting life cycle, but a complete description would be beyond the scope of this paper. Adult ticks are found on trees and underbrush usually from March to July, and occasionally as late as September. During dry, hot weather they seek the ground. It may be interesting to relate this fact to the cases being reported here. The area surrounding Estes Park in the summer of 1955 was cool and rainy during the months of June and August and was hot and dry during July. It was observed from the history of these cases that all except three were infected during June and the first week of July, the latter three during the month of August in the second rainy bout. According to the literature,[8] the peak occurrence is usually in late May and early June.

The geographical distribution of Colorado tick fever follows the distribution of the wood tick, Dermacentor andersoni Stiles.[6,10,23,30,32] The virus has been isolated from infected patients in California, Colorado, Idaho, Montana, Nevada, Oregon, Utah, Washington, and Wyoming. The relative occurrence in these states from a series of 193 patients from whom the virus was isolated by the Rocky Mountain Laboratories, Hamilton, Montana[6] (1948-1954) is as follows: (1) Idaho—52, (2) Colorado—38, (3) Nevada—34, (4) Oregon—26, (5) Wyoming—19, (6) Montana—16, (7) Utah—6, (8) California and Washington—1 each. The virus has been isolated from ticks in all of these states, thus making the disease endemic in the wood tick-infested areas of the above named states.

The popularity of the known endemic area of Colorado tick fever as a vacationland, the incubation period, and the speed of modern transportation are factors that make it possible for this disease to appear in any part of the United States or adjoining countries. Although the virus has been isolated from the dog tick in Long Island,[10,11] no naturally-occurring cases of the disease from this vector in the dog or human have been reported in the literature.

Persons affected by the disease are those whose occupational or recreational activities bring them in contact with the wood tick, such as cattlemen, sheepmen, foresters, fishermen, and tourists. The disease is noted most often in visitors to the tick-infested areas and is relatively uncommon in the natives of these areas. This fact is borne out in the clinical series presented in this paper, as there were only two natives and five summer residents among the 18 cases in this study. Patients in this series listed their homes in seven states other than Colorado.

Incubation Period

It will be noticed from this series (Table I) and from the literature that all patients give a history of having been bitten by a tick, of having had a tick

TABLE II
SYMPTOMATOLOGY AND PHYSICAL FINDINGS

Symptom	*No. Having*	*Physical Findings*	*No. Having*
Fever	18	Fever	18
Chilliness	18	Tachycardia	18
Malaise	18	Conjunctival Injection	14
Anorexia	18	Pharyngeal Injection	12
Muscular and joint pains	17	Hyperesthesia	9
Headache	13	Inflamed tympanic membrane and pharynx	2
Deep ocular pain	11	External otitis	1
Smoking—bad taste	7		
Photophobia	7		
Nausea	5		
Dizziness	4		
Constipation	4		

on their bodies, or of having been in a tick-infested area. The average incubation period in this series was about three days. However, it is difficult to obtain a reliable history as most patients do not know when the tick first became attached because it may be embedded in the body several days before it is first noticed. This is demonstrated by two patients who came to the clinic with typical symptoms, but ticks had not been found embedded in the skin until a careful physical examination had been performed. Thus the figure of three days is actually the average interval of time between the finding of the tick and the appearance of symptoms. Reports of this disease in the literature[6,10,16,23,27,29] generally state that the usual incubation period is four to five days. However, Florio et al.[13] found the incubation period to be only three days in human volunteers injected with infected serum.

Symptomatology

Although Toomey (1931)[29-31] lists a number of prodromal symptoms, I found no such prodromata. On the contrary, I was impressed by the sudden onset of symptoms. The patient could usually name the hour in which the symptoms began, even if at night. Within an hour, almost all of the symptoms had appeared. These patients were conscious of the onset of fever which alternated with a sense of chilliness, but not a true chill. The oral temperature in these patients varied from 99.4 to 103.2 degrees Fahrenheit (in many, the temperature was undoubtedly lowered by the salicylates which had been taken previous to the clinic visit). Other observers state that the temperature reaches a peak of 102 to 104 degrees Fahrenheit within the first 24 hours of symptoms.

With the onset of fever, the patient begins to have various muscle aches, which usually progress to marked muscular and joint pains throughout the body, particularly in the neck, back, and legs. A headache, which may be diffuse but is usually frontal in location and of varying severity, accompanies the onset. Within a short time the patient is overcome with a feeling of malaise and anorexia. For example, one patient was hungry shortly before mealtime, but by mealtime had considerable disinterest in food following the onset of symptoms. Other variable symptoms which soon may develop are deep ocular pain, photophobia, vertigo, nausea, vomiting, constipation, and a bad taste during smoking.

Course of Disease

These symptoms last 36 to 96 hours, the usual being about 48 hours. The average time for the first bout in this series was 56 hours (Table III). This was followed by a remission during which the patient was afebrile, often with a marked subnormal temperature, but was anorexic and had varying degrees of malaise. This remission lasts 24 to 72 hours, with an average length in this series of 53 hours. This average

TABLE III
COURSE OF DISEASE

Case No.	*Approximate Duration of* FIRST BOUT	REMISSION	SECOND BOUT
1	48 hours	72 hours	48 hours
2	56 hours	30 hours	72 hours
3	54 hours	24 hours	30 hours
4	36 hours	60 hours	36 hours
5	48 hours	48 hours	36 hours
6	72 hours	72 hours	36 hours
7	48 hours	72 hours	48 hours
8	60 hours	*	
9	60 hours	72 hours	48 hours
10	72 hours	60 hours	72 hours
11	48 hours	36 hours	48 hours†
12	48 hours		None
13	48 hours	48 hours	36 hours
14	48 hours		None
15	72 hours	48 hours	36 hours
16	48 hours	*	
17	96 hours		None
18	48 hours	48 hours	48 hours
Average	56 hours	53 hours	46 hours

* Patient discontinued treatment in remission.
† Patient No. 11 had a second remission of 36 hours, then a third bout lasted 48 hours.

excludes any patients who discontinued treatment during the remission and those who apparently had only one bout. The remission in most cases is followed by an exacerbation of symptoms similar to those found during the first bout. The second temperature rise gives the so-called saddle-back type of temperature curve. The duration of this second bout may be similar to the first, but in this data the average duration was approximately 46 hours in those 13 patients in whom we observed a second bout. Occasionally the patient may have only one bout, and rarely there may be three febrile bouts. The former was observed in 3 of the 16 adequately observed patients, and the latter was observed in only one patient.

Following the second bout the average patient slowly regains his appetite, but he may be weak for a varying length of time. Schaeffer[27] stated that the malaise is greater between the two bouts, and that only a day or two of weakness follows the second bout. According to Florio,[14,16] the patient feels tired for only a few days after the second bout. In following these 13 cases with second bouts, I observed that a marked weakness lasted for many days after the second bout in most cases. This is also the finding of Lloyd.[23] The malaise is said to be similar to that of dengue or influenza.[9,15]

Physical Findings

The relative absence of physical signs is a striking feature of this disease. All of these patients show an elevated temperature, the degree of which was described previously. Other findings include those that usually accompany a fever as: tachycardia, flushed facies, conjunctival and pharyngeal injection of varying degrees (see Table II). Occasional patients exhibit hyperesthesia over the sore muscles.

Toomey[29,30] states that the tips of the liver and spleen become palpable; however, other recent investigators do not report this finding. I was unable to palpate the liver or spleen on any of these 18 patients, even with diligent palpation. Although the lymph nodes do not become enlarged in uncomplicated Colorado tick fever, two of these patients (Cases No. 8 and No. 9) also exhibited the findings of acute pharyngitis and otitis media with cervical lymphadenopathy during the first bout. However, in view of the excellent response to penicillin therapy, the history and course of these cases (one showed a typical Colorado tick fever recurrence and the other left the city during the remission), the blood picture, and the presence of antibodies in the one patient, the diagnosis of Colorado tick fever, complicated by a bacterial infection (presumably streptococcal), was made. Another patient (Case No. 12) developed an external otitis about one week after the onset of Colorado tick fever. It seems most probable that the viral disease lowered the patient's resistance to other infectious diseases.

Prognosis

The prognosis in Colorado tick fever is excellent. I have been unable to find in the literature any report of a death due to proved or suspected Colorado tick fever. The patients are left quite weak temporarily, but all eventually regain their normal health and strength.

Laboratory Findings

Marked leukopenia is one of the significant findings in Colorado tick fever. There is a fall in the white blood cell count which, according to most authorities,[9,23,28] falls below 3,000 per cubic millimeter. The minimum count is usually reached during the second bout. One to four white blood counts were done on each of the patients in this series. Not all had counts that fell below 3,000, and I was unable to obtain a sufficient number of blood counts to make any valid conclusions. The average minimum white blood count was 3,255. A number of the patients in whom sufficient counts were obtained had minimum counts below 3,000 (eight of the 18 patients), and one patient's white blood count fell to 1,150. However, all had a minimum white blood count of 5,000 or less. Following the second febrile bout, the white count slowly returned to normal. Routine red cell counts were not done on these 18 patients. There is no change in the red cell count, according to the literature.

Although there are considerable individual variations in the differential counts, my studies on these patients showed a relative increase of 11 to 35 per cent in the lymphocyte count in eight of the ten patients with multiple hemograms. There was little significant change in the stab forms and a relative decrease in the segmented forms of polymorphonuclear leukocytes. There is considerable variation in reports on the differential counts in the literature.[17,23,28] Urinalyses in six of these cases were entirely within normal limits.

Complement-fixing[5] and neutralizing antibodies appear in human blood sometime between the ninth and 14th day of the illness and have been demonstrated to be present as long as 34 months later. The specific complement-fixing antigens for Colorado tick fever have been prepared from infected mouse brains. These tests have been shown by numerous investigators[5,9,22,26] to be specific for Colorado tick fever.

Single serum specimens were obtained from 11 of the 18 patients. Acute specimens were drawn on only

three of these. These three acute specimens showed no neutralizing antibodies, but the virus of Colorado tick fever was isolated in two of these specimens (through error, no attempt was made to isolate the virus in the third specimen). The virus is reported to be present in the blood during either the first or second febrile episode.[16,17] Convalescent specimens were obtained at from four to seven weeks after the onset of the disease in eight patients. The remaining patients left the area before convalescent specimens were obtained. Although only one specimen was obtained on each of these eight patients, the demonstration of high antibody titer in a single specimen is probably significant of recent infection with Colorado tick fever, especially when the patient came from outside the endemic area, or gave a reliable negative history for this disease. It is recognized that a definite rise in antibody titer is necessary to establish the diagnosis accurately. However, in view of the difficulty of obtaining numerous blood specimens in this transient type of clinic patient, and considering the typical clinical picture, the author believes that these high titers are confirmatory diagnostic aids for the purpose of this paper.

Case Histories

The following case histories and laboratory findings will serve to specifically illustrate the course of Colorado tick fever.

Case No. 5, H. E. H. This patient was a 17-year-old white male from Florida who was working as a waiter near Estes Park. He was first seen in the clinic on June 15, 1955, with the history that he had found two ticks embedded in his skin on June 10. About two hours before coming to the clinic he had the sudden onset of symptoms of fever, chilliness, headache, sore back, and malaise.

Examination showed an oral temperature of 99.8 degrees Fahrenheit and a pulse of 100. The laboratory findings are listed below. On the following day the patient had, in addition to the above symptoms, anorexia, deep ocular pain, and marked muscle soreness. He had a temperature of 100 degrees Fahrenheit (after salicylate therapy) and associated findings of a mild conjunctivitis and flushed facies. On the third day of his illness the only symptoms were anorexia, backache, and malaise. Temperature was 98.4 degrees Fahrenheit, pulse was 64. The next day the patient felt well enough to return to work, feeling only slight malaise, and his appetite was returning.

About noon on June 19, 1955, the patient suffered a relapse with sudden onset of fever, chilliness, generalized muscle and joint aches, anorexia, and malaise. Physical examination was again negative except for a temperature of 100 degrees Fahrenheit and mild associated findings. On the following day the patient's only symptom was malaise. Throughout the course of the disease there were no further findings on physical examination other than those noted in Table IV.

Case No. 18, H. J. This was a 43-year-old white woman whose home borders the tick-infested areas. She was certain that she had never had Colorado tick fever before. On August 22, 1955, she discovered a tick embedded in her skin and she thought it had become embedded the previous day. About 8:30 A.M. on August 22, she had the sudden onset of fever and alternating chilly sensations, headache, deep ocular pain, muscular and backaches, malaise, slight nausea, anorexia, and a "hot throat."

Physical examination at the first clinic visit revealed temperature of 101.2 degrees Fahrenheit, pulse of 110, and slight erythema of the pharynx. These symptoms continued into the night, and then the fever suddenly broke early the next morning. When she was seen in the clinic on August 23 the only symptoms were anorexia, malaise, and mild muscular aches; she had a temperature of 98.4 degrees Fahrenheit with no physical findings. During the next two days the patient's appetite improved and the malaise and muscular aches decreased. On the fifth day of her illness she suffered a relapse with symptoms of fever and alternating chilliness, headache, muscle and backaches, malaise, deep ocular pain, and anorexia. The only physical findings were a temperature of 100.8 degrees Fahrenheit, slight injection of the conjunctiva and pharynx, and a flushed

TABLE IV

WHITE BLOOD CELL STUDIES

Date	*WBC*	*% PMN*	*% Segmentors*	*% Band*	*% Lymphocytes*	*% Monocytes*	*% Eosinophils*	*% Basophils*
6-15-55	7800	71	69	2	20	3	6	0
6-16-55	4900	68	64	4	31	1	0	0
6-17-55	4600							
6-19-55	5100	77	74	3	18	1	4	0

TABLE V
WHITE BLOOD CELL STUDIES

Date	*WBC*	*% PMN*	*% Segmentors*	*% Band*	*% Lymphocytes*	*% Monocytes*	*% Eosinophils*	*% Basophils*
8-22-55	9450							
8-23-55	4600	67	62	5	27	3	3	0
8-24-55	4500							
8-26-55	4900							

facies. The following day the only symptoms were the decreasing anorexia, malaise, and muscular pains.

On August 22 a blood specimen was drawn and sent to the laboratory for analysis (Table V). The presence of the virus of Colorado tick fever was reported, and the specimen was entirely negative for neutralizing antibodies.

Immunity

None of these 18 patients gave a history of previous illness that could be called Colorado tick fever. Only two were native to tick-infested areas. This can certainly be taken to indicate that the majority of people native to tick country have at one time had Colorado tick fever and are now immune to the disease. Most of those having the disease are from areas foreign to the vector of Colorado tick fever. No individual has been known to have an authentic infection of Colorado tick fever a second time. Numerous investigators[9,13,15,16] have tried unsuccessfully to develop the disease a second time in human volunteers who have previously had the disease. With this in mind, there have been experimental attempts[21,22] to immunize volunteers against Colorado tick fever with an attenuated virus. Individuals have been successfully immunized, but only by means of suffering to varying degrees a minor case of Colorado tick fever. Thus it was decided that the effects of immunization for such a benign disease are of too little benefit to be used for the public.

Treatment

Since there is no successful anti-viral therapy, treatment consists primarily of symptomatic and supportive therapy with salicylates, codeine, and various other pain and muscle spasm relievers. In most patients we used desoxycorticosterone acetate in daily dosages of 7 to 10 milligrams, given intra-muscularly, for the duration of the symptoms. This was used with the idea that this cortical hormone helped the patient meet the stress of the disease and improved his sense of well-being. Our observations, although far from being objective, led us to believe that the morbidity of the disease was lessened by this drug. Since no controlled studies were done, however, no valid conclusions can be drawn on the use of desoxycorticosterone acetate in patients having Colorado tick fever.

Diagnosis

The history of sudden onset of fever, chilly sensation, anorexia, malaise, headache, backache, and generalized muscular aches, following the recent bite of a wood tick or in a patient who has been in a tick-infested area, should lead one to think of Colorado tick fever. The absence of rash or physical findings, other than those accompanying a fever, is significant in the diagnosis of Colorado tick fever. A white blood count taken on the first day of the illness will usually be within normal limits, but on the second day the leukopenia points out the viral etiology of the disease. The disappearance of fever and symptoms on the third or fourth day, with relapse one or two days later, makes the clinical diagnosis of Colorado tick fever presumptive unless proved otherwise. The clinical diagnosis can be confirmed by drawing a specimen of blood during one of the febrile periods and sending it to the laboratory for viral isolation.* After about the tenth day the presence of an increasing titer of complement-fixation and neutralizing antibodies is also diagnostic.

Differential Diagnosis

Although Colorado tick fever was formerly thought to be a mild form of Rocky Mountain spotted fever, it should not be confused with this much more severe disease. In Rocky Mountain spotted fever the characteristic exanthema makes its appearance between the second and sixth febrile day. This disease does not have the saddle-back course of fever and symptomatology seen in Colorado tick fever; rather, the fever continues from 15 to 20 days. Furthermore, this disease shows a leukocytosis rather than a leukopenia. The entire course of the disease is much more severe and prolonged than in Colorado tick fever.

Another viral disease with similar symptomatology

* This service is performed free of charge by Department of Health, Education, and Welfare; U. S. Public Health Service; Rocky Mountain Laboratory, Hamilton, Montana.

is influenza. One important consideration in differentiating this from Colorado tick fever is that influenza usually occurs in an epidemic form, whereas Colorado tick fever is strictly endemic. Furthermore, influenza usually occurs in the fall, winter and early spring, while Colorado tick fever occurs only during the tick season in the late spring and summer. Symptoms referable to the respiratory tract are common in influenza and almost never found in Colorado tick fever. Although the leukocyte count in influenza is low or normal, it is not uncommon for it to be slightly elevated; in Colorado tick fever, a moderate to marked leukopenia is the rule.

The course and symptomatology of dengue are similar to those of Colorado tick fever, but the geographical distribution of the two diseases is different; the former appears in tropical and sub-tropical countries, where it is transmitted by the Aëdes aegypti mosquito. Also, dengue has a characteristic rash. Viral and antibody studies further differentiate the two diseases.

Perhaps other viral diseases may at first be confused with Colorado tick fever, but they should readily be ruled out after close observation of the course, symptomatology, and physical and laboratory findings.

Prevention

Since no satisfactory method of immunization has been developed, prevention of Colorado tick fever is best accomplished by avoidance of the wood tick. Any attempt to rid an area of the wood tick would obviously be impractical and improbable. If one plans to enter a tick-infested area, it is advisable that he wear suitable clothing such as high boots, leggings, or socks worn outside the trouser legs; thus it will be more difficult for the tick to become attached. Even if dressed properly, a person should check his body and clothing for ticks several times each day to prevent their becoming embedded in the skin, particularly the hairy areas.

Summary

Colorado tick fever has been described for over a century, but the present name was established only 25 years ago. In the last decade it has been proved to be a separate disease entity, and the vector has been proved to be the wood tick, Dermacentor andersoni Stiles. The virus has been isolated and has been successfully transmitted in a number of laboratory animals.

The reported pathological findings are limited to the changes in the spleen of the golden hamster.

The geographic distribution of Colorado tick fever follows the distribution of the wood tick which is chiefly in the western mountainous states.

Eighteen cases of Colorado tick fever were observed during the summer of 1955 in Estes Park. Clinical, physical, and laboratory findings are reported. No attempt was made to draw any conclusions or add any findings from this limited study.

The disease is characterized by the history of contact with a wood tick and the sudden onset of symptoms of fever, chilly sensation, malaise, anorexia, headache, muscular aches and pains, and a number of less consistent symptoms. The saddle-back course of fever and symptoms is characteristic. Physical examination is characteristically negative except for fever and findings accompanying fever. The main laboratory finding is marked leukopenia. The virus can be isolated from the blood during the acute phase, and complement-fixation and neutralizing antibodies are found during the convalescent phase.

Diagnosis of Colorado tick fever is made on the basis of history of exposure to the tick, characteristic symptomatology, absence of physical findings except those accompanying a fever, and characteristic laboratory findings. Treatment is at present only symptomatic. Prevention is best accomplished by avoidance of the tick.

Acknowledgements

I wish to thank J. O. Mall, M.D., Estes Park, for the use of his facilities and for his cooperation and interest which have made this study possible. I also wish to thank Rickard C. Kennedy, medical bacteriologist, and the National Microbiological Institute, Rocky Mountain Laboratory, Hamilton, Montana, for work on viral isolations and serological tests.

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(Continued on Page 462)

PRESIDENT'S PAGE

DEAR DOCTOR:

There is need for better understanding of the much misunderstood Joint Commission on Accreditation of Hospitals. The able direction of Dr. Kenneth B. Babcock has produced an important instrument for maintenance of high quality of medical care.

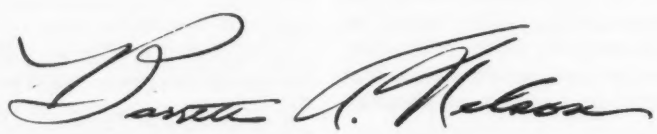
Doctors who comprehend the aims of the commission recognize its effectiveness in supporting the actively vigorous processes of self-examination and self-discipline evident throughout organized medicine; that the commission is largely composed of and in control of doctors of medicine; that it is not a policing body; that it is merely a policy making unit which crystallizes principles of good medical practice and systematizes the rules by which a hospital staff may voluntarily promote and encourage high standards of conduct among its own members.

True, there have been, in the past, hospital surveyors who lacked tact and helpfulness and understanding, even arousing resentment and antagonism instead of co-operation. As now organized, however, the surveyors are largely under Dr. Babcock's direction, and staffs are learning that the aim of the surveyor is to point up the areas where there can be effective improvement in conduct of practice.

Actually, most resistance and antagonism toward the commission rules result from mistaken and ill-advised actions of the hospital staff committees, especially record and tissue committees. Human nature being as it is, too many of us when placed in authority think we must browbeat and coerce. As one misguided chairman put it, "whip the doctors into line." Such methods effectively defeat the desired purposes. Likewise the mistaken thought that there must be multiplicity of forms and charts to complicate hospital records, or that nurses must be directed to spy upon doctors and file reports of supposed malfeasance and misconduct. When staff executive committees, committee chairmen, and hospital administrators are astute and understanding, they successfully obtain cooperation of staffs by tact and diplomacy and explanation, not by police methods enforced by either committees, administrators, or nursing staff. When hospital staffs understand the purpose and intent of the recommended rules, they invariably offer co-operative support. The few who fail to comprehend the importance of high standards soon learn that it pays to go along with the sincerely conscientious majority. The process is entirely democratic and commendable.

Our re-organized Committee on Hospitals is instructed to study the existing and future commission rules, interpret and disseminate them to our membership, and further, to act as a liaison to channel to the commission our thoughts on modifications for additional impetus to effective raising and maintenance of high standards of medical practice.

Fraternally yours,



President

EDITORIAL COMMENT

Whither, When, and Why

During the 1957 annual meeting of the Society, there were expressions of dissatisfaction with the trend of our meetings. These complaints were heard from members of the Society, and also from several of the exhibitors. One of these exhibitors even said that he could not recommend to the company he represents that they again have an exhibit next year, since attendance and interest were so low. Quite a number of members expressed rather strong feelings about the gradual decline of our meetings during recent years.

The subjects of these complaints are not new. There have been similar rumblings for several years, and no accusing finger should be pointed at the members in any one of the cities in which our meetings have been held. It has been a "trend" (whatever that is!), and we seem to be caught up in the stream along with other organizations and the attitudes of the day.

Our meetings have been excellent ones in the past—outstanding among state meetings according to some of the exhibitors who attended others. Comparison of our programs with other state meeting programs has left the impression that we had a superior scientific program, and interest has been high among our members. What has happened to cause a change in this situation? Why are our present meetings less attractive than earlier ones?

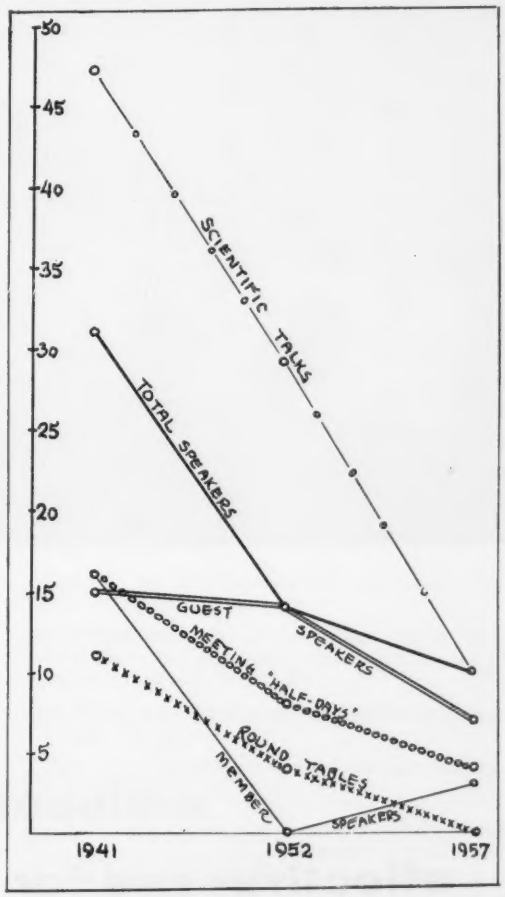
There are three essential parts of the annual sessions of the past: the scientific program, the business meetings (House of Delegates), and fun. The "fun" element has been drawing larger numbers of participants in recent years than before. Certainly the House of Delegates has been occupying more and more time, and in more and more prominent parts of our meeting days, so a shortage of this could hardly be considered the reason for lack of interest. This leaves for consideration the scientific program, and with this we can afford to make some study.

For purposes of comparison and to get an idea of changes in program policy, the programs of several representative years were studied. The years 1941, 1952, and 1957 were more or less arbitrarily selected for comparison, the first being representative of the era preceding World War II, and the two latter dates being representative of changes since World War II. The findings reveal some rather startling facts which are outlined briefly here.

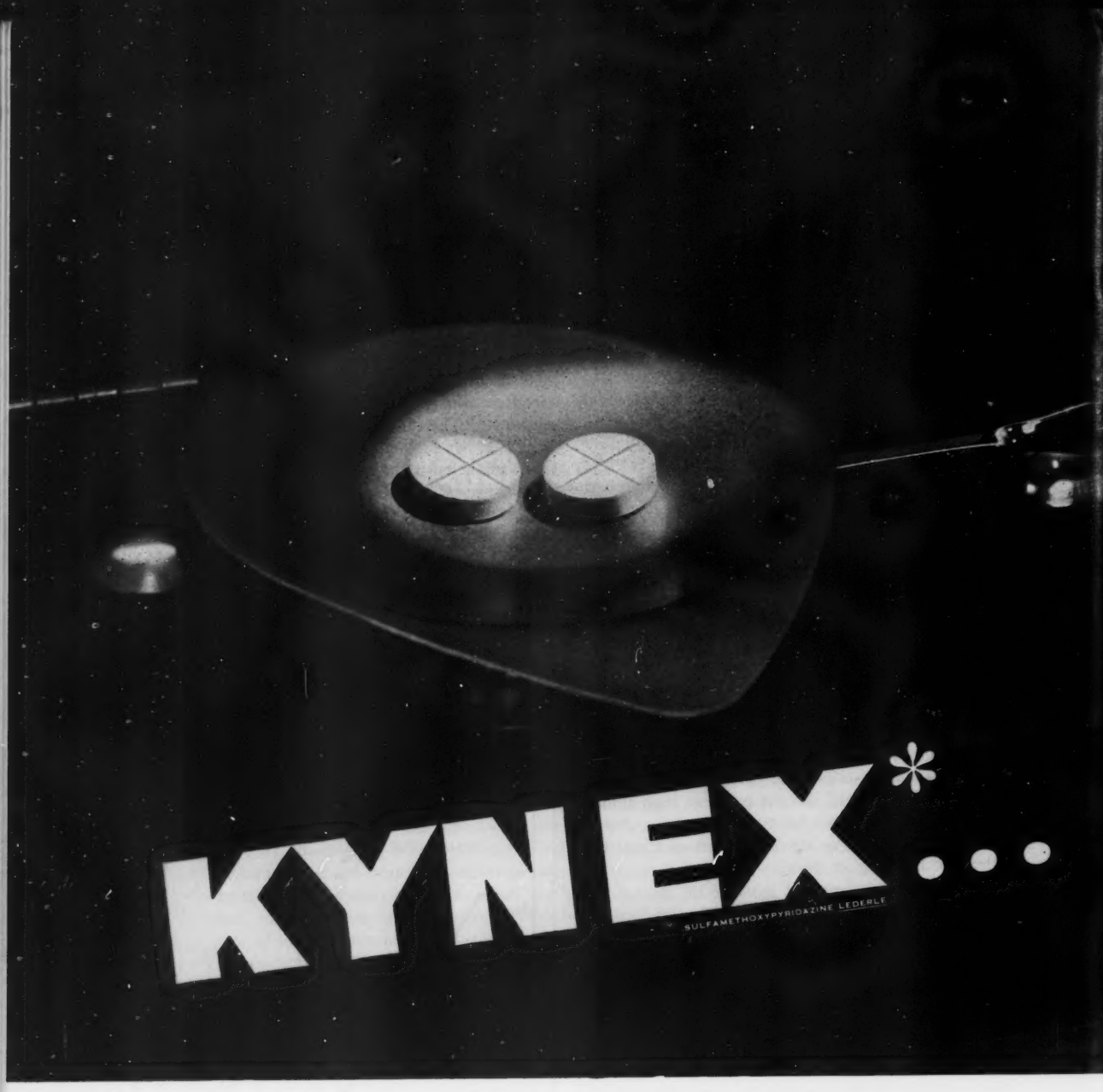
In 1941 the general program occupied three full days, with three simultaneous sectional meetings during the mornings and "general sessions" during the afternoons. In addition the EENT section had its own two-day meeting. This made a total of 16 "meeting half-days"—sectional and general. There were 47 scientific talks, given by 15 guest speakers and 16 in-state members, and there were 11 round-table luncheons—three or four each day!

In 1952 there were general sessions for two and one-half days, plus a Thursday afternoon clinical symposium at KUMC—actually still a three-day meeting. The EENT section had its meeting through two days again, but there were no other sectional meetings. There were 14 guest speakers who presented 29 scientific talks (eight of these by the two EENT speakers!). There were two round-table luncheons.

In 1957 we had 10 scientific talks (one of which was actually on a quasi-medical subject), presented by seven guest speakers and three in-state members during three general sessions. There were two panel discussions making up a fourth general session, and there was one noon-luncheon clinical pathological conference. There were no round-table luncheons,



A graphic analysis of the number of scientific events at state meetings during recent years.



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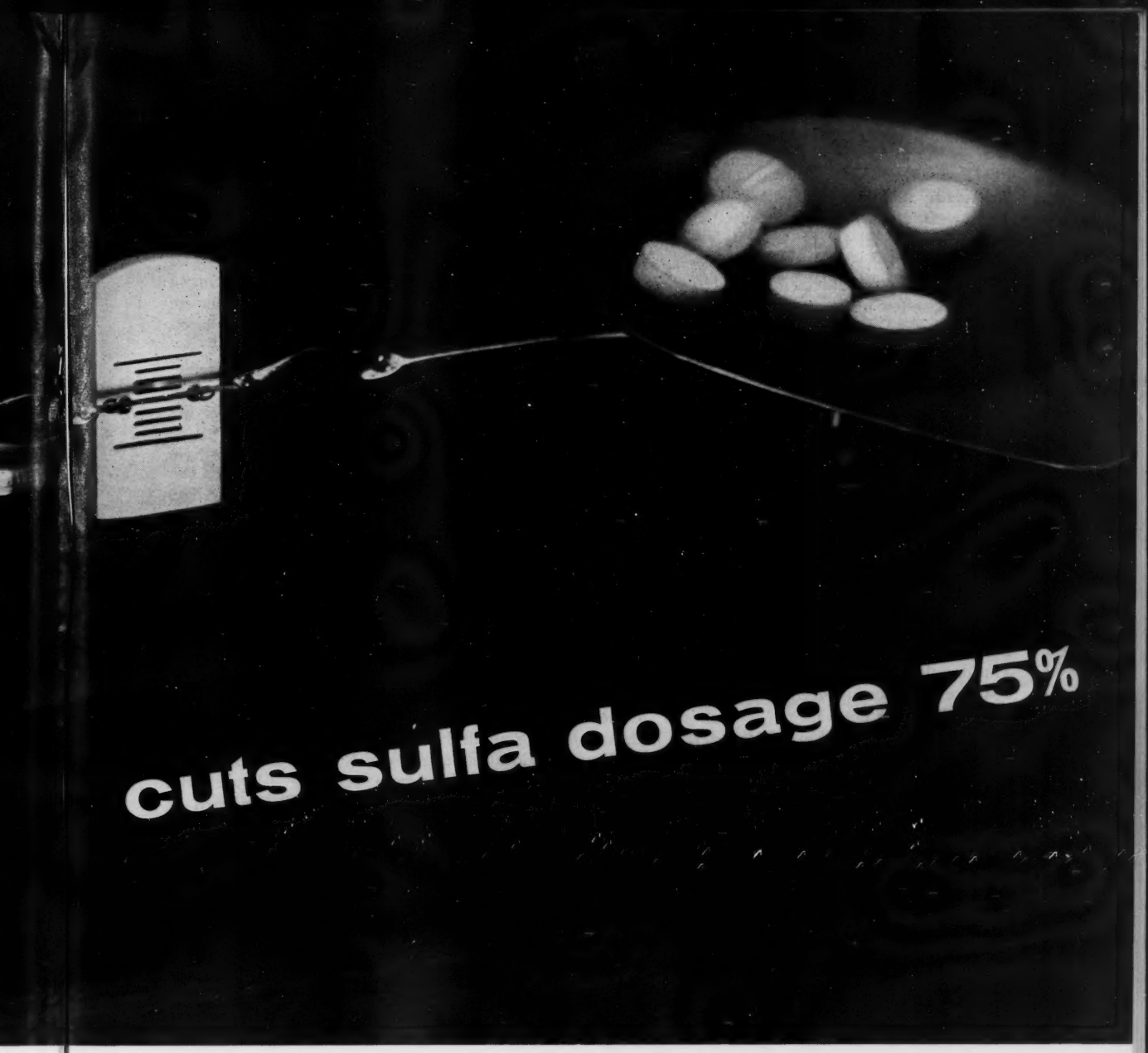

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1. Boger, W. P.; Strickland, C. S. and Gylfe, J. M.: Antibiot. Med. & Clin. Ther. 3:378 (Nov.) 1956.

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and for the first time in many years there was no EENT session. House of Delegates meetings occupied the Tuesday morning and Thursday afternoon hours which were formerly part of the scientific program.

Since impressions of the 1957 meeting are fresh in memory, some further reactions can be offered. The speakers were good and their talks were good, but there were so few of them that interest in the over-all program was never generated to a high degree. At the time that one guest speaker was to talk (he had come some 1,500 miles for the purpose), there were 19 people in the auditorium—including the speaker, the presiding officer, and the man who was to operate the projection equipment! By delaying the introduction some 15 minutes his audience had increased to 50—by actual count! As this speaker—one of the most outstanding of our guests—left the meeting place he was unaccompanied, and was obviously displeased, as he well had a right to be. In extending courtesy to one of our honored (?) guests, on this occasion we seem to have hit an all-time low. Do you think he or anyone to whom he relates his experience is likely to want to come to another of our meetings? We are not building up a good reputation by this sort of action. (Incidentally, the next speaker on the program had an audience of 35 for his excellent presentation.)

Perhaps we do not want to "go backward" to the type of meetings we had in pre-World War II days; perhaps there should be a further "progression" in the direction which is already being followed. Regardless of how one feels about this, it is strongly suggestive that there is more than a coincident relationship between less attractive meetings and less interest in the session as a whole. It strongly supports the view of most of us that a scientific program is the central core of a meeting and is the thing which creates the meeting interest and attendance. The idea still persists that doctors are more likely to congregate in large numbers for a good scientific program than they are to assemble for a golf tournament, a trap-shoot, or a lively House of Delegates meeting.

A number of excellent organizational meetings have no exhibits and prove to be well attended and enjoyed. This is true particularly of specialty organizations. The exhibits at our meetings serve a double and mutually advantageous purpose—affording us an opportunity to get information about products and equipment (while the dealers have an opportunity to advertise their products to a concentrated audience) and furnishing a significant portion of the meeting revenue. We probably want to continue to have exhibits, but if we do we will have to have an attractive meeting to get them.

Reasons for the change in policy of programs are not hard to find. In the first place it takes a great deal of work—thinking and planning, writing letters or telephoning, committee meetings, etc.—to arrange a good scientific program. There are now many other meetings of large societies and desirable speakers are in great demand, which makes it more difficult to get them for such meetings as ours. There are these many meetings for each of us to attend, and it is easy to argue, "Why bother to make our state meeting a strong scientific meeting when so many others are available? They won't come anyway; too many meetings to attend without this one."

So, of course, the easiest way out is to put together enough of a program to "get by," but it turns out to be one which is not too stimulating and does not attract much interest of our members. The "trend" has started; on it goes, and where it leads we have discovered.

What is to be done about it? What alternatives are there? Obviously many things have changed since 1941, and the type of program which was considered a good one then may well be entirely unsuited to the present. Some other possibilities come to mind, however, and are worth at least some consideration.

Of course we can continue as we are now doing. That is the easiest way at present, but seeing where it leads, how many will be satisfied to do that? A second possibility is to eliminate altogether the scientific program, and have the annual session be only a business meeting of the House of Delegates, perhaps with a recreational meeting. Probably such a meeting would command the attendance of those delegates who accepted their responsibility and felt obligated to attend, and would attract a few enthusiastic golfers or trap-shooters who wanted to have an annual game with some confreres in other parts of the state. But does it increase any Society enthusiasm or cohesion; or make us able to treat our patients any better? Obviously not.

A third possibility which has been suggested is to completely divorce the business meeting of the House of Delegates and the scientific program—have them at different times and probably in different locations. This would eliminate conflicts so that business of the Society would receive proper and undivided attention, and the scientific program would not be competing with other features for attendance of members. It would have to be a good meeting to "stand on its own feet," but this might be a satisfactory solution.

A fourth possibility is to retrace a little and concentrate on having an exceptional scientific program without having it conflict with the House of Delegates meetings. In 1957 the House of Delegates meetings occupied the Tuesday morning and Thursday afternoon spots which formerly were devoted to scientific program. Consequently, we had only four "half-days" of program as against six during earlier

years (and there were three and four programs going on at once during some of these six half-days). It seems that our organization is not large enough to have a House of Delegates meeting coincident with a scientific program, so we should make sure that such meetings do not conflict—even if we have to have them in different months.

Some have also suggested that all the scientific program be sectional in character. This is within reason, though it would "take a little doing." The section of general practice could be sponsored by the Kansas Chapter of the American Academy of General Practice; the surgical section by the Kansas Chapter of the American College of Surgeons; sections on internal medicine, obstetrics and gynecology, orthopedic surgery, anesthesia, cardiovascular diseases, etc., each sponsored by the appropriate group within our Society. Such meetings could be going on simultaneously without producing the serious conflicts occasioned by House of Delegates meetings competing with general sessions, and might be the answer to increased interest. They would, of course, be small meetings, but would still have to be of good quality, with featured speakers, if they were to fulfill our requirement.

Perhaps we need a drastic revision of our traditional procedures for the annual session. More continuity might offer some aid, as keeping the same group (or one undergoing gradual changes) responsible for scientific programs for an indefinite number of years. The contacts of one year's efforts are often a help for the next year's program. Such gains should not be deliberately thrown away. Various other committees of the Society are relatively stable from year to year. Why not a Program Committee?

Some of the possibilities that should be considered for future meetings could not be effected without changing some of our By-Laws, but that seems to be easily accomplished if we can judge from recent meetings of the House of Delegates.

Many members would like to see this Kansas Medical Society meeting become a high point of our year —and they believe it could, with some concerted efforts.

How the Other Half Lives

Professor Edward Turner of the Massachusetts Institute of Technology, who is now devoting most of his time to the World Health Organization in the field of sanitation, recently spoke to a Kansas audience.

He tried to impress upon them the difference between the standard of living in the United States and in much of the world, especially in those countries we classify as the Orient. He tried to present a picture of the vast number of people who live under circumstances that appear almost unbelievable to Americans. He said:

More people live in huts of straw or mud than any other type of dwelling.

More people travel on their own feet or by burro than by any other mode of transportation.

More people have a life expectancy of half our own than greater than our own.

More mothers watch at least one-half their children die than raise to maturity all those that are born to them.

More people are born, live all their lives, and die without the help of a person with a degree of doctor of medicine than those who have medical doctors to help them.

More people eat only what they grow or catch or kill than those who eat food processed by others.

More people do not know what it means to vote than have ever voted.

One begins to ponder over what effort would be required to overcome the centuries of inertia that have settled over such populations—what force would be needed to lift them into the flow of scientific development—and who is going to do it.

Leading Causes of Death

Even though the information is not new to physicians, it might serve a purpose to occasionally record statistics on changes in the leading causes of death in the United States. The following is paraphrased from a publication of the Health Information Foundation. The figures represent the years 1900 to 1954 and include roughly, as is seen, the first half of the 20th century.

The death rate from pneumonia has declined 86 per cent during those years from a place where 12 per cent of the total deaths were from this cause to the 1954 figure of 1 per cent.

Tuberculosis declined 94 per cent. Had the 1900 death rate prevailed to this date, at least 283,000 additional persons would have died of this cause by 1954. The decline in tuberculosis deaths appears to be accelerating in spite of an apparent contrary trend in Kansas, as suggested by the recent survey by Dr. Stocklen. Nationally there were 17,000 fewer deaths from tuberculosis in 1954 than in 1950, a reduction of 50 per cent.

In 1900 diarrhea and other gastrointestinal conditions ranked third among all causes of death. Since that date the reduction is 96 per cent. Diphtheria, during the same period, has declined 99 per cent. Had the 1900 figure prevailed in 1954, there would have been about 65,000 diphtheria deaths instead of the actual 200. Bronchitis was also among the first ten causes of death in 1900 and has been reduced by

96 per cent. In 1954 the death rate from bronchitis was 2 per 100,000 population.

In 1900 the communicable diseases among the first 10 causes of death accounted for 36 per cent of the total deaths and had a combined rate of 596.5 per 100,000, while in 1954 the rate for the same diseases was 46.3. This is a reduction of 92 per cent.

Today, as is well known, the so called degenerative diseases and accidents are the major causes of death. Heart disease resulted in more than 550,000 deaths in 1954. The 1900 rate per 100,000 was 137.4. In 1954 it was 315, an increase of 129 per cent.

This one cause alone took 37 per cent of the total, which is a higher proportion than the top three causes could account for in 1900.

There were nearly 237,000 deaths from cancer in the United States in 1954, and that figure is continuing to rise. In 1900 cancer accounted for 4 per cent of the total deaths; in 1954, 16 per cent of all deaths were due to this cause.

Accidents rank fourth for the total population but are first among all causes of death for the ages 1 through 24. Accidents caused the death in 1954 of 34 per cent of all deaths in the age group of 1 through 14 and 52 per cent of the deaths in the ages 15 through 24. Beyond 25 years of age, according to this survey, the relative importance of accident mortality decreases as age increases.

The report closes with a public reminder that diseases which frequently do not cause death still require much medical care and lead to time loss and inconvenience.

"As a result, the changing patterns in causes of death bring greater responsibilities to the individual in terms of his own health. These responsibilities—a better understanding of why we should seek medical care at the time it will be of greatest value and the necessity of budgeting to meet the costs of care—are within the primary objectives of Health Information Foundation.

"Foundation research aims to increase public knowledge of health services, for example, and to stimulate the growth of voluntary health insurance. Research is also aimed at assisting the many voluntary health insurance agencies in this country in their efforts to offer broader protection against the high costs of long-term illness. It is the Foundation's hope that *Progress in Health Services* contributes to the meeting of these objectives and to more general knowledge of mortality and morbidity and their implications."—*George Bugbee, President.*

More than 41 per cent of the deaths and more than 35 per cent of the injuries due to motor vehicle accidents last year occurred on Saturdays and Sundays.

Colorado Tick Fever

(Continued from Page 455)

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Clinicopathological Conference

Vomiting, Anemia, Confusion, and Convulsions

Case Presentation

Our discussion for today concerns a 52-year-old white male who entered the Medical Center on January 2, 1957, with vomiting and generalized pruritus and who died on January 6, 1957.

In 1953 he developed an aching in the back of his neck. This was recurrent for the next six months. After this he developed migratory arthritis with pain, swelling, and stiffness of the toes, ankles, knees, wrists, and hands. Until December, 1955, his treatment consisted of aspirin and weekly injections of vitamins. From December, 1955, to August, 1956, he received 5 mg. of prednisone three to four times daily, and his arthritis was improved.

On August 21, 1956, he developed a severe headache with nausea, weakness, vomiting, and confusion, and he was hospitalized elsewhere on August 28. He had two convulsions that evening. During that hospitalization he was confused and irrational. Treatment was symptomatic, and his family was told he had encephalitis. He suddenly became rational after two and one-half weeks, and he was discharged. At that time capsules of vitamin D were given three times a day in place of prednisone. He improved for one week, but progressive nausea, weakness, and nervousness again developed, and vomiting and generalized pruritus occurred in December, 1956. He was given chlorpromazine and amobarbital for the nausea. He drank three or four glasses of milk and orange juice daily in the hope that it would facilitate his recovery.

The patient had been a chronic alcoholic from 16 to 44 years of age, but he had had no alcohol since 1949. In 1952 he had epigastric pain which was relieved by food and antacids, and he was told that he had an ulcer. He obtained some relief of pain with prednisone.

He was a well-developed, well-nourished, pale, white man who appeared to be chronically ill. His pulse was 80 and regular; the blood pressure was 170/95; respiration, 20. He was edentulous. A few spider nevi were noted over the upper anterior chest. The lungs were clear, and there were no cardiac murmurs. The kidneys, liver, and spleen were not felt. There was an easily reducible right inguinal hernia and a trace of pretibial edema. There was effusion into both knees, greater on the left, with some ankle swelling and fusiform swelling of the fingers. There was some limited motion of the knees, but no pain. He was lethargic, and his memory for recent events was poor.

The specific gravity of the urine was 1.005; reaction, alkaline; 1 plus albumin; negative sugar. There were many disintegrated granular and waxy casts and pus cells. The red count was 3,120,000 with 9.0 gm. of hemoglobin. The white count was 7,150 with 61 per cent polymorphonuclears, 28 per cent lymphocytes, 40 per cent eosinophiles and 7 per cent monocytes. The platelet count was 289,000. The VDRL was non-reactive. The blood urea nitrogen was 52 mg. per cent; creatinine, 6.4 mg. per cent; uric acid, 6.1 mg. per cent; glucose, 85 mg. per cent; carbon dioxide, 28 mEq/L; sodium, 139 mEq; potassium, 4.6 mEq; chloride, 88 mEq; calcium, 6.0 mEq; phosphorus, 2.6 mEq. The serum albumin was 4.41 gm. per cent, and the globulin was 2.39 gm. per cent. A hepatogram showed a total serum bilirubin of 0.4 mg. per cent; alkaline phosphatase, 1.7 millimole units; urine urobilinogen, 0.6 mg; cephalin cholesterol, negative; thymol turbidity, 18 units; total cholesterol, 198 mg. per cent with 70 per cent esters. The serum transaminase was 9 GOT units; serum iron, 80 gamma per cent; ammonia, 80 gamma per cent; zinc turbidity, 9 units; and the 24-hour urinary calcium excretion was 5.7 mEq. Sulkowitch's test was normal. Bence Jones protein was not found in the urine. The sedimentation rate was 33 mm. in 15 minutes and 35 mm. in 60 minutes.

The patient continued to be lethargic and nauseated but showed some improvement after receiving promazine and a suspension of aluminum hydroxide with magnesium trisilicate. He took fluids well. On January 4 his intake was 5600 ml., and his urinary output was 2200 ml. On January 5 he drank 1500 ml. of water. That evening he complained of headache and nausea, and at 11:00 p.m. he had a grand mal convulsion. From 11:00 p.m. to 6:05 a.m. on January 6 he had numerous seizures which could not be controlled with intravenous amobarbital. Immediately after the last seizure he became cyanotic and died.

Dr. Mahlon Delp (moderator): Are there any questions?

Dr. William Larsen (hematologist): Was the blood pH done?

Edited by Jesse D. Rising, M.D., and Mahlon Delp, M.D., from recordings of the conference participated in by the departments of medicine, pediatrics, surgery, radiology, and pathology of the University of Kansas Medical Center as well as by the third and fourth year classes of medical students.

Dr. John Schmaus (medicine resident): No.

Dr. Larsen: Was there any brown pigmentation of the skin?

Dr. Schmaus: No.

Dr. Larsen: Had his blood pressure been high?

Dr. Schmaus: We do not know about his blood pressure before his admission here.

Dr. Larsen: Was a bone marrow examination done here?

Dr. Schmaus: No.

Charles R. Phipps (fourth year medical student):* How many times did he vomit?

Dr. Schmaus: He vomited twice on the evening of January 4, and the next day he became progressively more restless and vomited three or four times.

Irving Ringdahl (fourth year medical student): Was there evidence of recent weight loss?

Dr. Schmaus: He had lost some weight, but I do not know how much.

Mr. Ringdahl: Was an encephalogram done?

Dr. Schmaus: He had grand mal convulsions following which he became cyanotic and expired, so no electroencephalogram could be done.

Robert Pettegrew (fourth year medical student): What amount of barbiturate did he receive the night preceding his death?

Dr. Schmaus: He received 200 mg. of amobarbital at 11:00 p.m. and another 200 mg. at 2:15 a.m.

* Though a medical student in February, 1957, when this conference occurred, he, like the others referred to as students, received the M.D. degree in June, 1957.

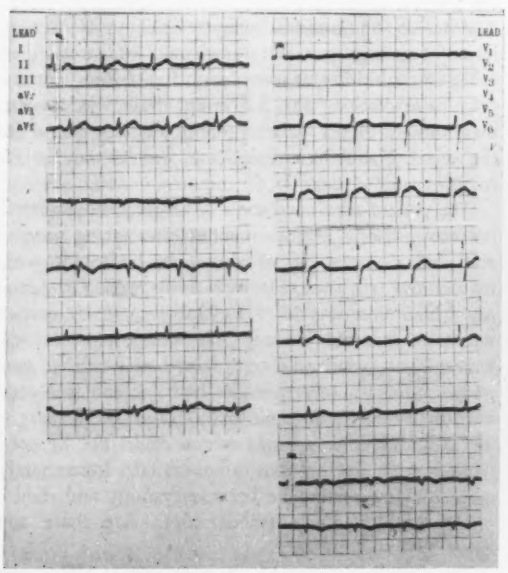

Figure 1. Electrocardiogram taken on admission.

Jack D. Reese (fourth year medical student): Was a spinal puncture done?

Dr. Schmaus: The spinal fluid pressure was normal. There were no cells. The sugar was 78 mg. per cent; the chloride was 712 mg. per cent; the protein, 52 mg. per cent; the serology was negative.

Eugene G. Peterson (fourth year medical student): How much vitamin D had he taken?

Dr. Delp: Probably about 50,000 units three times a day.

Mr. Peterson: Did he have any other vitamin injection?

Dr. Schmaus: Probably B_{12}.

Mr. Phipps: Was he hypertensive?

Dr. Delp: I do not think so.

Mr. Peterson: What was his occupation?

Dr. Delp: He ran a grain elevator.

Mr. Phipps: Were there any abnormal neurological signs?

Dr. Schmaus: Nothing aside from his tremor.

Dr. Delp: May we see the electrocardiogram please.

Mr. Peterson: We have the electrocardiogram which was taken upon admission (Figure 1). The rhythm is normal, and the rate is 80. I can see no abnormality of the P-R or Q-T intervals, nor any evidence of ischemia. I interpret this as a normal electrocardiogram.

Dr. Delp: We will now have the x-rays.

Mr. Ringdahl: The chest x-ray was taken on January 2. The heart appears to be slightly enlarged, and there are increased hilar markings, but I interpret it as being essentially normal. The upper gastrointestinal x-rays were made on the same day, and there appears to be an ulcer on the greater curvature side of the duodenal bulb. The x-ray shows the shadows of the psoas muscles and the outlines of the kidneys. I

Figure 2. X-ray film of the hands.

see no evidence of any abnormality. The film of the hands (Figure 2) shows fusiform swelling of the fingers. The x-ray of the skull is essentially normal.

Dr. Delp: Dr. Youngstrom, do you have any comments?

Dr. Karl Youngstrom (radiologist): The hands show some fibrocystic changes in the subchondral zone and in the distal end of the ulna. The teeth show some abscesses (Figure 3).

Dr. Delp: May we have the discussion, please, Mr. Phipps?

Differential Diagnosis

Mr. Phipps: The case we are discussing today is that of a 52-year-old white male who was admitted on January 2, 1957, with a complaint of generalized pruritus and vomiting. He was well until 1953 when he developed arthritis, and his treatment over two years consisted of vitamins. From December, 1955, to August, 1956, he was given prednisone with some relief. He received vitamin D three times a day for five months before his death. Four months before his admission he developed weakness, nausea, and vomiting, and he was hospitalized and treated symptomatically with temporary relief. After his dismissal his symptoms became gradually worse, and he was admitted to this hospital.

During his hospital course he was given promazine and aluminum hydroxide with magnesium trisilicate. On this regimen he improved for a time. He took fluids well. Three days before death his intake was 5600 ml., and his output was 1200 ml. On the day before death he drank approximately 1500 ml. of water. That evening he complained of headache and vomited. He then had a grand mal seizure, followed by several other seizures which were not controlled with amobarbital. Immediately following the last seizure, he became cyanotic and died.

I shall base my differential diagnosis on anemia, azotemia, and hypercalcemia. The first disease that I want to consider is sarcoidosis. This is relatively rare. Twenty to 40 per cent of these patients have hypercalcemia. The manifestations of the disease depend upon its location, which may include the kidneys. Bone lesions and skin lesions are common. Hyperglobulinemia and anemia may be present. I rule this out on the basis of the absence of adenopathy, the lack of x-ray findings, and the presence of a normal serum globulin.

Multiple myeloma is a disease which occurs most commonly after the age of 40 and is found frequently in males. Anemia is common. Characteristically the patients have severe pain from involvement of the bones and the red marrow. Kidney damage is not unusual. Hypercalcemia is found in 50 per cent of all cases. Bence Jones protein appears in about 30 per cent, and hyperglobulinemia is usually present. I rule this out because of the absence of hyperglobulinemia, Bence Jones protein, and typical bone lesions.

Primary hyperparathyroidism appears most often in middle life. About 10 per cent of the reported cases are females. Ninety per cent of the cases are intraparathyroid adenomas; the remainder are caused by parathyroid hyperplasia and carcinoma. Bone lesions are usually present, and calcific deposits in the renal tissue are common. The presenting symptoms may be those of renal insufficiency or calculi. Weakness, anorexia, vomiting, weight loss, and constipation are usually present. Urinary calcium and phosphorus are increased. The serum alkaline phosphatase is increased; bone phosphorus is decreased. I rule this out on the basis of normal alkaline phosphatase and lack of x-ray findings.

Secondary hyperparathyroidism due to chronic renal disease has to be considered. This is due to increased retention of phosphorus by the diseased kidney, with an associated high circulating calcium re-

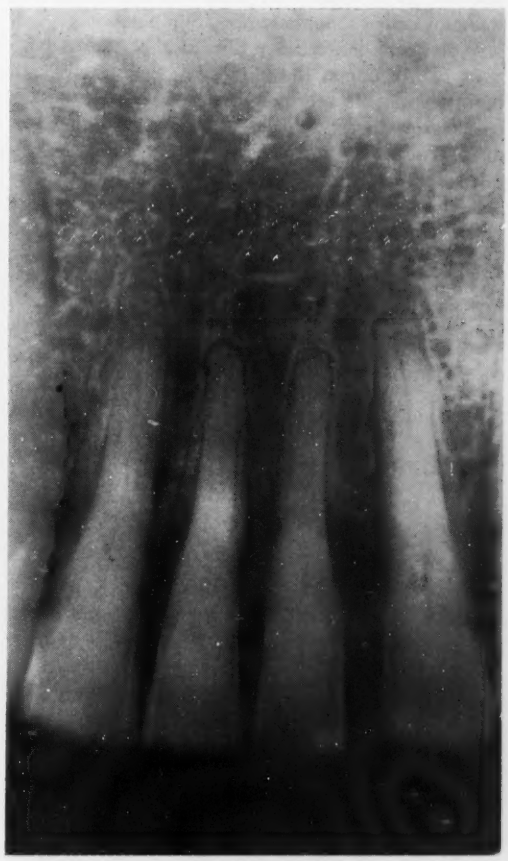

Figure 3. X-ray film of the teeth.

sulting in the stimulation of the parathyroid. Because of normal alkaline phosphatase and x-rays and the absence of initial renal disease, I rule this out.

A recent addition to hypercalcemic disturbances is Burnett's syndrome caused by the excessive intake of milk and alkali. This was first described in 1949 as milk-alkali syndrome. It is characterized by hypercalcemia without hypercalcinuria, change in the alkaline phosphatase or in the serum inorganic phosphorus. The clinical symptoms are not unlike those presented in the protocol. A history of increased and excessive intake of milk and alkali are in favor of this diagnosis. This history could not be definitely ascertained from the patient, so I cannot definitely rule this out.

The last entity to consider is hypervitaminosis D, which occurs in patients who have used the vitamin excessively and injudiciously. The symptoms are many, including the following: weakness, fatigue, weight loss, nausea, vomiting, cramps, diarrhea, headache, vertigo, depression, and psychoses. The patients have increased serum calcium and phosphorus and normal or slightly elevated alkaline phosphatase. Radiologically abnormal calcification may be observed. Renal insufficiency due to abnormal depositions of calcium in the kidneys is almost universal. Normocytic, normochromic anemia is present in various degrees in all patients who have renal involvement. The dosage required to produce this effect is calculated at about 100,000 units daily, but the development of symptoms depends not only on the dose but also on the individual susceptibility of the patient. Treatment consists of stopping the drug, low calcium diet, and high fluid intake. I believe that this patient had hypervitaminosis D. Furthermore, I believe that he had iatrogenic peptic ulcer as a result of the treatment of his arthritis with prednisone, and that he died in status epilepticus with anoxia of the vital centers and subsequent cardiac and respiratory failure.

Clinical Discussion

Dr. Delp: Thank you. Mr. Ringdahl, what is your diagnosis?

Mr. Ringdahl: Hypervitaminosis D.

Dr. Delp: Any second diagnosis?

Mr. Ringdahl: Well, it is difficult to rule out hyperparathyroidism.

Dr. Delp: Mr. Peterson?

Mr. Peterson: I was under the impression that he got into a condition of subclinical milk-alkali syndrome with nephrocalcinosis. This would make it easier for him to get hypervitaminosis D.

Dr. Delp: What about the physical findings?

Mr. Peterson: He had the familiar weakness, weight loss, and general confusion.

Dr. Delp: Any other physical findings?

Mr. Peterson: I should expect calcium deposits in most of the viscera, probably in the subcutaneous tissues or around the knees, but these probably could not be found upon physical examination.

Dr. Delp: What about his anemia?

Mr. Reese: That can probably be explained on the basis of azotemia.

Dr. Delp: How do you explain the patients's convulsions?

Mr. Pettegrew: They could also be due to azotemia.

Dr. Delp: Mr. Phipps?

Mr. Phipps: I think that the convulsions could also be due to cerebral edema.

Dr. Delp: Mr. Reese?

Mr. Reese: I think that anoxia may have been a factor.

Dr. Delp: Mr. Ringdahl?

Mr. Ringdahl: I think they may be explained on the basis of hypercalcemia.

Dr. Delp: What about his nausea and vomiting and gastrointestinal troubles?

Mr. Ringdahl: Azotemia.

Dr. Delp: Now, you are not going to explain everything on the basis of azotemia.

Mr. Pettegrew: This may be due to the toxicity of vitamin D.

Dr. Delp: If this is such a toxic substance, how does it accomplish its toxicity?

Mr. Pettegrew: The increase in vitamin D intake may lead to increase of calcium absorption and increased serum calcium, which may induce the parathyroid gland to elaborate more parathormone. This decreases the excretion of phosphorus. The increased level of calcium and phosphorus in the blood may lead to the toxicity.

Dr. Delp: How do you explain the fact that this man told me repeatedly that his ulcer pain was relieved by taking prednisone?

Mr. Phipps: I think that his relief was probably due to his mental state, because prednisone should aggravate the ulcer.

Dr. Delp: What caused the patient's death?

Mr. Peterson: Cerebral hypoxia.

Dr. Delp: Why was he cyanotic?

Mr. Ringdahl: Because of his status epilepticus.

Dr. Delp: You know this man was walking about at 6:00 p.m. the evening before his death. At 7:30 he started vomiting. What caused his death?

Mr. Reese: Probably cerebral edema.

Dr. Delp: Dr. Rankin?

Dr. Thomas J. Rankin (internist): This man had four difficulties. He had a rheumatoid arthritis-like syndrome. We must accept his duodenal ulcer, and from his history of alcoholism and finding of spider nevi we can expect some diffuse hepatic fibrosis. He had chronic renal disease, which, from the laboratory work in the protocol, might well have been chronic pyelonephritis. The question is whether any of these

diseases had any complications which could have caused neurological symptoms and resulted in his death. Could any of his medications have caused complications which led to his neurological death, or could he have had a completely different entity? I do not believe that his hepatic disease had enough complications to lead to his death, nor do I believe that his renal disease had enough complications to do so.

We are left with the differential diagnosis of a primary rheumatoid-like disease and its complications and therapy. Hypervitaminosis D is an attractive diagnosis except that the protocol said that he had nausea, vomiting, weakness, and confusion before he received the vitamin. He was started on vitamin D about August 1, probably because they could not think of any other remedy to relieve his symptoms, and they were afraid to continue with prednisone.

I cannot explain primary disturbance of calcium metabolism by hyperparathyroidism because of the negative findings in the laboratory. A recent article[3] on the treatment of rheumatoid arthritis gives the maximum safe daily maintenance dose of prednisone as 9 mg. for men, 7½ mg. for premenopausal women, and 5 mg. for postmenopausal women.

I do not like the concept of the milk-alkali syndrome, when the man's alkali was limited to nonabsorbable alkali. I am attracted by another alternative; perhaps the rheumatoid-like syndrome was but a reflection of a more serious disease.

Dr. Delp: Dr. Azarnoff, do you agree with the diagnosis of hypervitaminosis D?

Dr. Daniel L. Azarnoff (resident in medicine): This man developed symptoms which might be attributed to a vitamin D excess, but vitamin D intoxication is rare. Although most people agree that one has to take about 150,000 units daily for a period of time, there was one case reported of a patient who received 100,000 units a day for two weeks and developed a fatal intoxication. If he had chronic renal disease and superimposed vitamin D intoxication, the terminal event could well be explained by the fact that he had excess fluid and developed pulmonary edema and died from that.

Dr. Delp: Dr. Wilson, can you explain this man's anemia on the basis of azotemia?

Dr. Sloan Wilson (hematologist): The degree of anemia depends upon the duration of the azotemia.

Dr. Delp: We might assume he had it for six months. Do you have any other explanation for his anemia?

Dr. Wilson: We do not know whether the man was hemolyzing or not.

Dr. Delp: Do you think that vitamin D intoxication in itself can cause anemia?

Dr. Wilson: I cannot answer that.

Dr. Delp: Dr. Christianson, what is your diagnosis?

Dr. John F. Christianson (internist): Hypervitaminosis D.

Dr. Delp: Dr. Allen?

Dr. Max Allen (internist): Cerebrovascular accident was the terminal event.

Dr. Delp: What was your diagnosis at the time, Dr. Weber?

Dr. Robert Weber (internist): My first diagnosis was multiple myeloma. I thought he probably also had vitamin D intoxication and milk-alkali syndrome. You probably wonder why the dental x-rays were shown: the lamina dura rules out hyperparathyroidism, and does leave the possibility of multiple myeloma.

Pathological Report

Dr. Chauncey G. Bly (pathologist): Although we are presenting the most plausible correlation of the findings on this patient, there are some areas in which there may be alternative interpretations.

A moderate degree of rheumatoid arthritis was noted in the fingers and knees. Although this represented the patient's primary disease process, it is of perhaps greater interest to consider the results of the treatment for this disease and the complications which contributed to his death. The most prominent of these results was the diffuse metastatic calcification of soft tissues, generally typical of the lesions following prolonged and excessive doses of vitamin D.

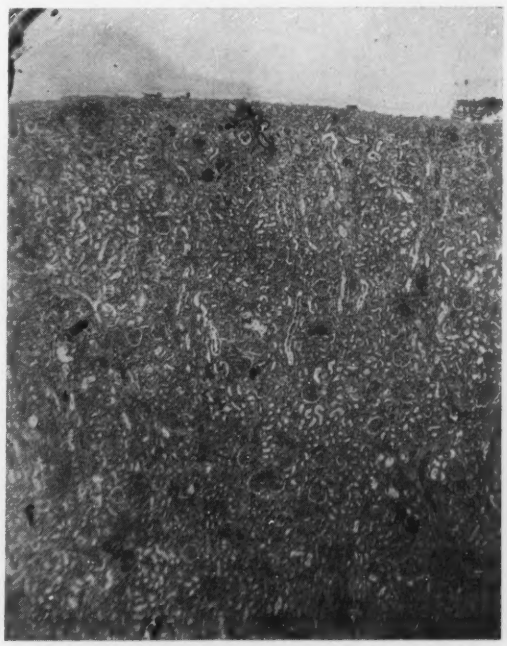

Figure 4. Nephrocalcinosis, at low power, shows widely disseminated foci of calcific precipitates in casts and tubular structures.

The kidneys weighed 360 gm. together and were grossly firm, pale, and fibrotic with an irregularly swollen cortex. A few rounded small grey-based scars grossly suggested chronic pyelonephritis. Microscopically, however, these areas of diffuse and focal chronic inflammation and fibrosis appeared to be related to numerous depositions of calcium salts. These were seen within the tubular epithelial cells, impregnating casts occluding tubular lumens, or thickly encrusting the basement membranes of arterioles or of tubules (Figures 4 and 5). As a result, the tubules showed widespread evidence of old and recent degeneration, with frequent peri-tubular fibrosis and occasional complete fibrous obliteration of the lumen. There were no grossly detectable calculi in the urinary tract.

Nephrocalcinosis is, of course, only one of the lesions possible when an excess of vitamin D upsets the normal control of the absorption, deposition, or excretion of both calcium and phosphorus by the body. The blood levels in this patient reflected this disturbance: the calcium values of 5.8-6.0 mEq/L (normal 4.5-5.5) and the phosphorus values of 2.6-2.8 mEq (normal 1.5-2.5) were elevated, tending to confirm hypervitaminosis D and to rule out both milk-alkali syndrome and hyperparathyroidism.

If a patient does not have a high level of serum globulins to solubilize the serum calcium, and our patient did not, one ordinarily expects to find soft tissue precipitates of calcium and phosphorus whenever their solubility product exceeds 10-13, using milliequivalents, or 30-40, using mg. per 100 ml.[1] The solubility product of the levels of calcium and phosphorus in this patient was about 16, so we were not surprised to find diffuse foci of calcification of soft tissues. There were many fine, granular calcifications in the base of the aortic valve. These were surrounded by acute and chronic inflammatory tissue, implying that these were of relatively recent origin, probably within the last few months of the patient's life. There were small calcium deposits in the lung, in the walls of various small arteries throughout the body, in the pia mater, in the sheath of the optic nerve, and in the dura (which contained several larger deposits). Many of the lymph nodes, including the mesenteric and the hilar nodes, contained fibrohyaline nodules, many of which were calcified, but these probably represented old chronic inflammatory disease. The aorta, retina, and sclera were free of precipitates.

Figure 5. Nephrocalcinosis, at high power, demonstrates extensive intertubular and intratubular fibrosis and interstitial chronic inflammatory cells.

One wondered whether these abnormal soft tissue mineral deposits reflected exogenous sources or represented excessive mobilization and depletion of endogenous sources, so the bone and marrow were examined to elucidate this point. The bone cells were quiescent and disappointingly inactive, suggesting that much of the soft-tissue calcium came from the diet rather than bone. Osteoblasts were found in several areas. Osteoclasts were uncommon, however, and were not located in typical Howship's lacunae, and therefore did not suggest the existence of hyperparathyroidism, either primary or secondary. Elements of all three series of marrow cells were present in normal proportions, and we found no explanation for the patient's anemia.

The heart was moderately enlarged to 410 gm., correlating with his clinical blood pressure of 165/95, but there was only slight secondary arteriolar sclerosis in the kidney. It is conceivable that the inflammatory reaction and scarring from the nephrocalcinosis produced enough renal ischemia to initiate the hypertension.

The brain was grossly swollen and edematous, weighing 1560 gm. Microscopically, sections of the brain demonstrated occasional peri-vascular cuffing with lymphocytes and small glial nodes and foci of chronic inflammatory cells within the brain substance, often near collections of small, spherical, bluish, hyaline "atrophy bodies," usually associated with focal or diffuse cerebral atrophy. Although these findings were not pathognomonic of encephalitis several months ago, they strongly supported that clinical history. No specific etiologic agent was indicated.

The patient had a small acute and chronic duodenal ulcer, 8 mm. in diameter, which showed no bleeding point. This ulcer seemed too small to have given

symptoms for five years, and it was not as large as many of those seen after several months of anti-inflammatory steroid therapy. Our patient's steroid therapy, however, was discontinued a few months before death. There was a small surface ulceration at the cardio-esophageal junction, beneath which there was peculiar arteriolar necrosis and extravasated blood. Most of these lesions seemed attributable to his terminal debility, uremia, and vomiting. Focal agonal hemorrhagic pancreatitis was also found but was not contributory to his death.

The lungs weighed 2270 gm. They were massively wet with diffuse edema, fibrinous uremic pneumonitis, and patches of acute hemorrhagic bronchopneumonia with massive exudates of polymorphonuclears filling small bronchi, and foci of acute terminal aspiration pneumonia with necrotizing digestion of pulmonary tissue. Numerous polymorphonuclears and bacteria in small vessels suggested the presence of a terminal bacillary septicemia with post-mortem over-growth. Small areas of fibroblastic organization of pneumonia were scattered throughout both lungs.

There were many older disease processes of isolated interest in the lungs. Scattered small, hyalinized, silico-fibrotic nodules contained doubly-retractile silicon needles, and may have been related to his work as a stonecutter 25 to 30 years before death. There were large numbers of disseminated small granulomas and fibrotic nodules containing foreign-body giant cells; because some of these contained bits of vegetable spores and debris, we were inclined to correlate them with his occupation as a grain elevator operator for the last 22 years of his life. In almost every alveolus we saw a few "dust cells" containing fine black and brownish-yellow pigment granules which correlated with his history of the consumption of nearly two packages of cigarettes a day. Finally, the almost ubiquitous Ghon complex of fibro-calcified nodules was present in the lungs and hilar nodes, although we were unable to demonstrate the organisms of either tuberculosis or histoplasmosis in the old lesions.

In summary, this patient was apparently treated with excessive amounts of vitamin D for rheumatoid arthritis. He developed nephrocalcinosis, possible renal hypertension and progressive uremia. The overhydration which he, himself, had carried on continued in the hospital. The subsequent cerebral and pulmonary edema, and the uremia, acute bronchopneumonia, vomiting, and aspiration pneumonia with cyanosis led to his death.

Dr. Delp: I, too, think that this was a case of vitamin D intoxication. There are other comments I would like to make. First of all, I suspect that we fail to recognize vitamin D intoxication rather frequently. Next, I think that we do not recognize the fact that hypercalcemia is associated with a set of symptoms practically never mentioned in textbooks, namely, gastrointestinal symptoms. I do not know whether the explanation is clear, but I am sure it must be the effect of the hypercalcemia on the vegetative nervous system. Finally, this patient was observed carefully for two days to see whether he was putting out enough urine, and then he was permitted to drink water in large amounts. We let him take too much water, and he developed cerebral edema. This precipitated his convulsive state, which we were not able to control. We worked ourselves into a dilemma by thinking that we could reclaim this patient.

Dr. Rankin: I would like to comment that vitamin D has no place in the management of arthritis.

Dr. Delp: We learned our lesson about vitamin D in 1939, '40 and '41. We treated osteoarthritic patients in this outpatient department with doses like this, and it did not take us long to find out that we were getting into trouble. We are extremely cautious about it now.

Summary

Dr. Delp: Nausea, vomiting, anemia, azotemia, hypercalcemia and convulsive seizures in a patient having arthritis represent a clinical syndrome which should immediately suggest the possibility of hypervitaminosis D. Quite certainly this is not a common situation, but it still occurs with a frequency sufficient to warrant caution in permitting indiscriminate self-medication with a substance quite benign when used properly.

In this instance renal failure had progressed beyond the point where water diuresis could reclaim the patient, and actually water intoxication probably precipitated the uncontrollable convulsive seizures.

Pathological Anatomical Diagnosis

Rheumatoid arthritis of fingers and knees.

Nephrocalcinosis and focal calcifications of soft tissues including the aortic valves and the pia mater.

Cardiac hypertrophy.

Arteriolonephrosclerosis, moderate.

Duodenal ulcer, acute and chronic.

Acute and organizing hemorrhagic bronchopneumonia, pleurisy, and focal acute aspiration pneumonia.

Acute and chronic massive pulmonary edema.

Possible uremic pneumonitis.

Cerebral edema, severe, and peripheral edema, slight.

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PHYSICIANS' ACTIVITIES

Dr. William J. Reals, Wichita, spoke on "The Spirit of Learning" before a meeting of the Catholic Hospital Association Council in Cleveland, May 27.

The American Urological Association announces that **Dr. M. D. McComas, Jr.,** Concordia, has been elected to membership.

Dr. Robert L. Mardock has left Wichita to establish a practice in Ouray, Colorado.

Two graduates of the University of Kansas School of Medicine who recently finished internships at Tacoma General Hospital, Tacoma, Washington, have announced plans to practice in Belleville. They are **Dr. Herbert D. Doubek** and **Dr. E. J. Chaney.**

Dr. Francis C. Newsom and **Dr. Bert E. Stofer,** Wichita, were among the speakers at the 12th annual Ministers and Physicians Clinic sponsored by Wesley Hospital and the Wichita Council of Churches recently.

Plans to move to Albany, Missouri, have been announced by **Dr. Charles M. Newman** of Axtell, who has been practicing there for more than 50 years.

Dr. Charles M. Poser, instructor in neurology at the University of Kansas Medical Center, presented a paper at a meeting of the American Neurological Association in Atlantic City on June 19. Later he went to Belgium where he addressed a meeting of the Annual Congress of Neurology in Brussels.

A preliminary program for the fall meeting of the Kansas City Southwest Clinical Society indicates that a number of members of the Kansas Medical Society will participate in panels and symposia, **Dr. William T. Sirridge, Dr. Albert N. Lemoine, Jr., Dr. Michael J. Ryan, Dr. Donald L. Rose, Dr. Sloan J. Wilson** and **Dr. Lee H. Leger,** all of Kansas City.

Dr. Francis N. Lohrenz, Newton, recently became a diplomate of the American Board of Internal Medicine.

Six physicians were recently appointed by the Topeka Board of Education, on advice of the Shawnee County Medical Society, to form a medical examining board for Topeka public schools, **Doctors Louis Cohen, Francis T. Collins, John E. Crary, Floyd C. Beelman, Robert H. O'Neil,** and **Don C. Wakeman.**

Dr. Murray C. Eddy, Hays, spoke on "The Doctor and the Medical Record Librarian" at a workshop sponsored by the Kansas Society of Medical Librarians in Hays last month.

Dr. W. Clarke Wescoe, dean of the University of Kansas School of Medicine, was recently appointed to a five-year term on the American Medical Association Council on Medical Education and Hospitals.

Plans to begin practice in Olathe have been announced by **Dr. Robert Delphia,** a recent graduate of the University of Kansas School of Medicine who served his internship at St. Joseph's Hospital, Kansas City, Missouri.

Dr. E. Grey Dimond, of the University of Kansas Medical Center, participated in a panel discussion on coronary artery disease at a program sponsored by the Southern Illinois Heart Association in Olney last month. From June 30 through July 7 he served as visiting chief pro-tem at the Atlantic City Hospital.

Winter Veterans Administration Hospital, Topeka, has announced the appointment of a new chief surgeon, **Dr. Louis F. V. P. Vanderhorst,** formerly with the VA hospital in Altoona, Pennsylvania. Dr. Vanderhorst is a graduate of the University of Utrecht in the Netherlands. He replaces **Dr. Joseph P. Bell,** who resigned from the Winter staff to enter private practice in Las Vegas.

Dr. Ivan W. Cain, Kansas City, was elected president of the Kansas State Board of Health last month.

A talk on diet was given by **Dr. George L. Thorpe,** Wichita, chairman of the A.M.A. Section on General Practice, at the A.M.A. meeting in New York last month.

Dr. Deryl D. Fuller, Marquette, has announced plans to move to Lindsborg when a new office building is constructed there.

Dr. M. S. Carney, Manhattan, has resigned her position as city-county health director to move to California. The work in Manhattan will be taken

over by **Dr. Patricia L. Grossman** of the Student Health Department at Kansas State College.

Medical assistants of Harvey County, meeting in Newton last month, heard a talk on thoracic surgery given by **Dr. Robert G. Rate,** Halstead.

Dr. Lee F. Kramer, formerly of Cherryvale, moved to Ohio on July 1 and is now practicing in Worthington, a suburb of Columbus.

A physician in Sumner County for 54 years, **Dr. Harry L. Cobean,** was honored at a party at the courthouse in Wellington recently on the occasion of his 85th birthday. He has served as county health officer for many years.

Dr. C. J. Kurth, Wichita, was elected president of the Guild of Catholic Psychiatrists at the organization's annual meeting in Chicago in May.

The American Academy of Microbiology has invited two physicians at the University of Kansas Medical Center, **Dr. Tom R. Hamilton** and **Dr. Noble P. Sherwood,** to be charter fellows.

"Typhoid fever" was the subject discussed by **Dr. Roscoe F. Morton,** Arkansas City, at a recent meeting of the Cowley County Medical Assistants' Society.

Dr. Paul H. Lorhan, of the University of Kansas Medical Center, served as an examiner for fellowship candidates of the American College of Anesthesiology in New York last month.

Plans for a proposed hospital in Northeast Johnson County were outlined by **Dr. Donald J. Smith,** Overland Park, at a recent meeting of the Johnson County Democratic Women's Club.

Dr. Roscoe F. Morton, Arkansas City, was named president-elect of the Kansas Heart Association at a meeting held in Wichita last month. **Dr. Don C. Wakeman,** Topeka, was elected vice-president.

Last month **Dr. R. T. Nichols,** Hiawatha, observed his 55th year in the practice of medicine. A feature story in the *Hiawatha Daily World* presented his biography and a tribute to his standing in the community.

An exhibit, "Surgical Pathology of the Esophagus, Stomach, and Duodenum," was presented at the A.M.A. meeting in New York City last month by a group from the Hertzler Clinic, Halstead, **Doctors William C. Dreese, Jack W. Welch, Victor E. Chesky, Robert G. Rate,** and **Christian A. Hellwig.**

BLUE SHIELD

A new method of non-group enrollment which permits application for membership by individuals at any time during the year was announced last month by Kansas Blue Cross-Blue Shield.

Dr. Francis Collins, president of Blue Shield, explains that this new continuous enrollment was made available especially for people who are unable to qualify through membership where they work or through association group enrollment.

This is the first time in the history of Blue Cross-Blue Shield in Kansas that a continuous statewide enrollment has been conducted. The Blue Cross-Blue Shield program now in effect for non-group members is the one which is being offered in the new continuous enrollment. It is the method of enrollment that is different, not the program itself.

It is the hope of Kansas Blue Shield that physicians will participate in promoting the non-group program by making use of enrollment material and informational literature which will be furnished them upon request.

This continuous type enrollment is being offered as a result of an experiment on that basis conducted last year in a number of counties. In those counties, the experiment was satisfactory as well as economical and for that reason is being expanded to the entire state.

Sedgwick County Elects Officers

Officers for 1958 were elected by members of the Sedgwick County Medical Society at a meeting held in Wichita last month. Dr. Edward S. Brinton was named president; Dr. Harold L. Low, vice-president; Dr. William H. Fritzemeier, secretary; Dr. Charles L. Gray, treasurer; Dr. Donald O. Howard, censor for a three-year term; Dr. Ernest W. Crow, Dr. Norton L. Francis, and Dr. William J. Reals, to the board of directors for three-year terms.

According to Health Information Foundation, the average American incurred total charges of $71.50 for medical care and services in 1956. In the same year, the average person covered by voluntary health insurance received benefits of $27.

A.M.A. House of Delegates Meeting

The 106th annual meeting of the American Medical Association held in New York City, June 3 to 7, was the largest in the history of the association. Over 55,000 individuals were registered, including over 19,000 physicians. The House of Delegates considered numerous problems without getting into quite as much controversy as in the past three sessions.

The revision of the Principles of Medical Ethics was passed as modified. It is consistent with the ideas of the Kansas Medical Society so was supported by your delegates. The House discussed and adopted a "Suggested Guides to Relationships between State and County Medical Societies and the United Mine Workers of America Welfare and Retirement Fund." The basic principle behind the guide is that beneficiaries under the fund should have good medical care and should be free to select their own physicians. It advocates a fee-for-service method of payment except under unusual circumstances. In approving the guides, the House also recommended that the Board of Trustees study the feasibility and possibility of setting up similar guides for relations with other third-party groups such as management and labor union plans.

The Medicare program was discussed, and the House took these actions. It condemned payments to or on behalf of residents or interns or house officers for services while in a training program. It suggested in future contract negotiations that the type of contract and the question of whether or not a fee schedule be included should be left to individual state determination, and restated the American Medical Association contention that the Dependent Medical Care Act does not require fixed fee schedules. It also suggested that the A.M.A. attempt to have existing Medicare regulations amended to incorporate the Association's policy that the practice of anesthesiology, pathology, radiology, and physical medicine constitute the practice of medicine, and that fees for services by physicians in these specialties should be paid to the physician rendering the services.

A couple of resolutions favoring compulsory inclusion of physicians in the Federal Social Security System were introduced. These were turned down and the House re-affirmed its opposition to compulsory coverage of physicians under the Old Age and Survivors Insurance provision of the Social Security Act.

Several miscellaneous actions were considered. The House urged a more careful screening of television and radio patent medicine advertisements. It directed the Board of Trustees to investigate the indiscriminate use of stimulants such as amphetamine in relation to athletic programs. It opposed the establishment of any further veterans' facilities for the care of non-service-connected illness.

It is a pleasure to report that Dr. Clarke Wescoe was elected to the Council on Medical Education and Hospitals.

George F. Gsell, M.D.
Lucien R. Pyle, M.D., Kansas Delegates

Officers for Clinic Managers' Group

Mr. W. M. Birthelmer, of the Wichita Clinic, was named chairman of the Kansas Association of Clinic Managers at the group's annual meeting in Wichita in May. Mr. John Polson, of the Hertzler Clinic at Halstead, was elected vice-chairman, and Mr. Ramon E. Eller, with Doctors Carr and Smiley in Junction City, was chosen to serve as secretary-treasurer. During the meeting the clinic managers heard a discussion of Medicare and a talk on fee schedules. Three panel discussions, on clinic procedures, credit and control, and accounting procedures, made up the rest of the program.

Associate Director at KUMC

Mr. Russell H. Miller has been named associate director of the University of Kansas Medical Center by the board of regents, succeeding Mr. Robert A. Molgren, who resigned recently to become administrator of St. Luke's Hospital in Kansas City, Missouri. Mr. Miller joined the staff of the Medical Center in August of 1952 as assistant administrator.

Each year, colds take an estimated economic toll of $2 billion in the United States alone. Any day in winter there are more than 20 million people suffering from a cold, according to the Kansas State Board of Health.

Gastric Acidity

(Continued from Page 445)

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THE MONTH IN WASHINGTON

Editor's Note. The following summary of Washington news was prepared by the Washington office of the A.M.A. for distribution to state and regional medical journals.

The 85th Congress is in the final few weeks of its first session with prospects that it will enact few major medical bills this year, but that next year will be a different story. On at least half a dozen important measures action has been postponed, with the understanding that the issues will be fought out in 1958.

Circumstances prevented any delay on one bill that is of considerable importance to the younger doctors—a new version of the doctor draft act. It had to be enacted by July 1, the Defense Department insisted, or not enough doctors would be available to maintain the military medical services at an acceptable level.

The problem is that the Armed Forces require a higher ratio of physicians to troops than exists between physicians and the general population. Without some special law, the services would either have to make out with fewer doctors than they say they need, or draft thousands of non-physicians merely to obtain the doctors who are in the particular age groups.

This scheme was devised: Amendment of the regular draft act to allow the call up, to age 35, of the necessary numbers of doctors from among those who had received educational deferments; they could be called because they are physicians, not because they are of a certain age. Also, the national, state and local Medical Advisory Committees of Selective Service would be continued, as would a number of provisions in the original act that protect the rights of drafted doctors.

As Congress moved toward adjournment, prospects also were that it would enact a bill to help out some states caught in a financial squeeze because of a new act, passed last year but not scheduled to go into effect until July 1, 1957, to increase federal payments for the medical care of persons on the state-federal public assistance rolls.

Under the old system, states could use the U.S. dollars to pay directly to the individuals for their medical care, or directly to the vendors of medical service—hospitals, physicians, dentists. Many states, adopting the second plan in all or part of their counties, used the federal money to help maintain pooled funds, which support various medical care programs.

All U.S. money paid out under the new act must be used in the form of vendor payments—that is, not turned over directly to the public assistance cases. At the same time, the law as originally passed stipulated that any money received under the old plan henceforth would have to be handled as "recipient payments," that is going directly to the persons on public assistance rolls.

A number of states thus faced the prospects of drastically revising their carefully-established medical care programs or sacrificing large amounts of federal money. Congress came to their rescue by means of a bill that would allow them to use the old money as before, yet take full advantage of the new federal program.

In the closing weeks of the session, however, two major medical bills were making little, if any progress—those for federal grants to medical colleges to build teaching facilities and for initiating a program of health insurance for federal civilian employees.

A number of bills had been introduced on aid to medical education, representing virtually all the viewpoints in Congress and the administration, but nothing much was happening. Here one factor was the economy drive, which was not too successful in cutting the administration's health budget, yet which virtually precluded any new programs involving large appropriations.

On federal employee health insurance, these long-standing differences of opinion still blocked any compromise: Should emphasis be on basic health insurance, or on major medical (catastrophic) coverage? Should U.S. payroll deductions be permitted, or would this open the door to demands for many other payroll deductions, such as for union dues? What safeguards could be set up to prevent either the commercial insurance companies or the nonprofit organizations (union plans and Blue Cross-Blue Shield) from gaining a dominant position?

On these two major bills, as well as on many others, sponsors were not too discouraged. Already they were making plans to press them still more vigorously next year when Congress, looking toward the fall elections, may be more responsive.

Doctors are asked by PHS to be on the alert for a new type A influenza strain expected to work its way into this country from the Far East. Details from state health departments.

National Library of Medicine officials were still hopeful, as the end of the session neared, that Congress would vote enough money to start constructing the library's new building next year.

Choline

A Review of Indications for Therapeutic Use

ROBERT G. GODFREY, *Kansas City*

The value of choline as an adjuvant to therapy involving human disease is a question that is as controversial as it is new. The use of choline and related substances as medicinal agents has hardly progressed beyond the experimental stage, yet there is extensive literature dealing with the subject.

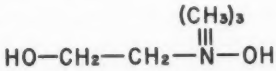
It is my purpose to present some of the conflicting views on this subject and to interweave these discussions with a consideration of more firmly established experimental work on the metabolism of choline and related substances. This is done in order that the reader may more accurately evaluate the possible potential of these agents in therapeutic applications.

Choline was first isolated from hog bile lecithin by Strecker in 1849, but for 75 years following this nothing was made of this discovery from a physiological standpoint. It was less than 25 years ago that the work of Banting and Best on insulin led to the recognition of the production of extremely fatty livers in depancreatized dogs maintained on adequate insulin therapy.

Upon more extensive investigation, Best and Hershey[8] found that fatty livers could be prevented by the administration of lecithin and that the active agent in lecithin was choline. This discovery, along with the finding that the ordinary albino rat was susceptible to liver steatosis produced by dietary choline deficiency, has been the basis of a vast amount of research which continues today.

The Nature and Occurrence of Choline

Choline is a quaternary base resembling ammonium hydroxide with a hydroxyethyl group replacing one hydrogen and three methyl groups replacing three other hydrogens. The formula for choline is



In pure form it is a colorless, crystalline, highly hygroscopic compound with a bitter taste. It is readily decomposed by heat to form trimethylamine and glycerine—a fact which aids in its chemical determination. Bacteria are able to decompose choline to form neurine, a highly poisonous substance.

Choline is found in nature. It occurs in most foods, and eggs are especially high in choline content. Dry beef or pork liver contains 2.0 per cent choline, and whole grain, yeast, and peanut meal are good sources. Choline is found in nature bound as part of the phospholipid molecule. Phospholipids are active lipids found universally in all living cells. They are composed of fatty acids, an alcohol, and phosphoric acid in conjunction with a nitrogen base—either choline or some other related lipotropic substance. Examples of phospholipids are the lecithins, sphingomyelins, and cephalins. The ubiquitous nature of the phospholipids indicates their being essential for either cell metabolism or cell structure or both. Since choline is an integral part of the phospholipid molecule, to establish the need for phospholipids is to establish the need for choline.

While there is little chance of an average adult developing a deficiency of choline, the knowledge of deficiency symptoms in lower animals has led many workers to regard choline as a vitamin. King[33] feels that choline is a member of the B-vitamin group, and Sure[47] and György and Goldblatt[25] concur in this opinion. Best, Mawson, McHenry, and Ridout[10] agree that it is an essential accessory food factor, but they hesitate to classify it as a true vitamin. McHenry[34] points out that according to strict definition it cannot be classified as such, for even though it does meet every qualification for a vitamin as regards its essential nature, it fails to meet the stipulation that a vitamin must be incapable of synthesis within the body.

The work of du Vigneaud and Stetten[18] conclusively proved that choline can be synthesized in vivo, providing certain equally essential precursors are present in the diet or within the body. Superficially this may appear to be pedantic "hair-splitting"; still, the elucidation of this seemingly minor point has

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This is one of a group of theses written by students at the University of Kansas School of Medicine, selected for publication by the Editorial Board from a group judged to be the best by the faculty at the school. Mr. Godfrey is now a third year student at the school.

The author wishes to acknowledge the interest and attention given him by Dr. Harold Edelhoch, assistant professor of oncology and biochemistry, University of Kansas School of Medicine, who acted as advisor in the preparation of this paper; and Dr. W. Clarke Wescoe, dean of the University of Kansas School of Medicine, who served as reviewer of the final manuscript.

Thanks also are due to Dr. D. J. Mulford, professor of biochemistry at the University of Kansas, under whose direction and guidance the author first became interested in the problems of choline metabolism, and who was kind enough to read the preliminary manuscript and offer valuable criticisms and suggestions for its improvement.

led to the unfolding of the process by which choline is synthesized and, in so doing, has opened the way for tremendous advances in all phases of metabolism involving the transfer of labile methyl groups, i.e., transmethylation.

These workers[18] using C^{14} and deuterium as tracers concluded that choline is synthesized in the body if ethanolamine and methionine are present in adequate amounts. Figure 1 shows the relationship between these substances and other related precursors and products.

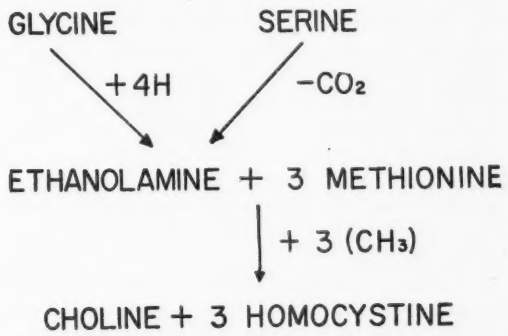

Figure 1. Synthesis of choline in vivo.[18]

Choline Deficiency

The rat has been the main font of knowledge concerning symptoms seen in choline deficiency. When fed a choline-deficient diet, rats show demonstrable changes within a matter of hours. Most intensively investigated has been the development of fatty livers (steatosis or fatty metamorphosis). It would appear that without choline the liver is unable to synthesize vital phospholipids or to oxidize fatty acids properly.[7, 15] As a result, when fat is absorbed and passed on to the liver, it is rapidly stored in this organ since it can neither be transported out as phospholipid, nor can it be oxidized for energy.

McHenry[34] points out that there are two types of lipid which are deposited in the liver in rat choline deficiency experiments: neutral fats (glycerides) and cholesterol esters. It should be remembered that there is a great difference in the nature of these two lipid fractions, for while choline is effective in the reduction of the glyceride moiety, it shows little or no effect on the reduction of cholesterol esters.[4, 7] Dragstedt, Prohaska, and Harms[17] have discovered a component of pancreatic extract which they call "lipocaic," capable of mobilizing cholesterol esters out of the liver. They feel this substance is a hormone; however, more recent work has demonstrated a similar substance in wheat germ, and Gavin and Sinclair[44] have shown inositol (a constituent of cephalins) to produce equivalent effects.

In addition, it should be noted here that the most recent experimental evidence indicates that there are two basic types of hepatic injury resulting from all experimental deficiency studies: first, there is fatty metamorphosis (involving either one or both of the gyceride and cholesterol fractions), and second, an overt cellular degeneration or necrosis. Daft[16] recognizes these as being two separate and distinct entities. Schwartz[40] points out that substances offering protection against one often enhance the production of the other. Hence, while choline, betaine, and B_{12} act to protect against fatty metamorphosis, they tend to enhance the production of liver necrosis. In the present discussion the primary concern shall be with the fatty metamorphosis syndrome.

In addition to liver injuries, it has been found that within six to eight days after the institution of a choline-deficient diet, rats develop what is termed by Griffith[22] the "hemorrhagic renal syndrome." This condition is characterized by extensive subcapsular and cortical hemorrhagic degeneration, involving both tubules and glomeruli of the kidney. Christensen[12] also notes other pathological lesions in the rat resulting from choline deficiency which include: involution of the thymus, enlargement and congestion of the spleen, blood in the lymph node sinuses, and ocular hemorrhages. Other experiments indicate choline to be important in rats for the production of normal epithelium[43] and lactation.[47] It is also effective in the prevention of perosis or "slipped-tendon" in chickens.[31] Choline deficiency manifestations have also been observed in dogs, rabbits, mice, and rhesus monkeys as well as in certain bacteria.

The exact meaning and importance of these many diversified findings have not been thoroughly interpreted; in fact, some have not even been speculated upon to any great extent. Still, choline has been implicated in every phase of metabolism including that of carbohydrate and protein[31] as well as fat. In addition, there are certain relationships between choline metabolism and the body's endocrine balance,[11] vitamin complement,[23, 34] mineral components,[2] general level of nutrition,[45] and even its environmental status.[42] Although the nature of these relationships is not all clear, it may be concluded with Griffith[22] that choline is essential not only for normal fat metabolism but also for tissue maintenance and animal survival as well.

It is readily seen that somewhere amidst this maze of findings there quite reasonably might be some correlation with disease states in man presenting similar symptomatologies. Should this be the case, it is not unreasonable to assume that some of these conditions might respond to choline therapy. In this respect, however, it is imperative that it be remembered that, because a bird will fly if thrown from a tall building, it does not necessarily follow that the same will hold true for a human subjected to the

same treatment. While analogies with experimental animals are valuable tools of research, we must always regard them with reservations awaiting final proof of their validity.

Lipotropic Action

Hepatic injuries. The development of fatty livers in human disease is not an uncommon occurrence. The normal mammalian liver contains about 5 per cent lipid; however, under pathological conditions, the level may rise as high as 20 to 30 per cent. In the human such livers are often seen in prolonged passive congestion, syphilis, alcoholism, and prolonged malarial fever. All these conditions are associated with cirrhosis of the liver concomitant with fatty metamorphosis. Poisonings due to carbon tetrachloride, phosphorus, arsenicals, chloroform, sulfonamides, and lead, as well as diabetes, yellow fever, eclampsia, hyperthyroidism, viral hepatitis, dietary deficiencies, severe burns, and carbohydrate deprivation, all cause cellular degeneration and necrosis subsequent to fatty metamorphosis. As McHenry puts it, "Any condition or agent which interferes with phospholipid turnover in the liver, interferes with fat metabolism and tends to cause accumulation of neutral fat and cholesterol esters."

A condition in man closely resembling prolonged experimental choline deficiency is diffuse nodular (Laennec's) cirrhosis of the liver. Choline has been tried both experimentally[25, 39] and clinically[15, 24] in the treatment of this pathological state; however, the complex etiology of cirrhosis makes comparison difficult, if not impossible. The results, therefore, have been variable. Although a certain degree of improvement has been observed by some workers,[15, 24] generally it has been found[31] that choline has little effect on cirrhosis once the disease has become well established. This is not surprising when one considers the nature of the disorder with its cellular destruction and fibrosis. As Jukes[31] concludes in his excellent review, once the liver has become shrunken and fibrotic, there is little chance of reversal towards normal. He goes on to say, however, that in spite of this discouraging note, choline or equivalent lipotropic therapy is often of value in supportive treatment of cirrhosis, for it has been found that choline may aid in lessening the progression of the disease or, once regression is established, hasten its resolution.

It is extremely interesting to note the striking resemblance between Laennec's cirrhosis and kwashiorkor (African protein deficiency disease). Daft[16] suggests that these diseases may be one and the same since dietary deficiencies appear to represent a common etiology for both. If this is true, kwashiorkor may be a relatively common dietary disease of worldwide distribution.

Choline deficiency may be related to still other hepatic disorders; some of these are summarized in Table I. These examples, again, supply evidence of the two basic types of liver injury, viz., fatty meta-

TABLE I

EFFECTS OF CHOLINE IN EXPERIMENTAL AND CLINICAL HEPATIC DISORDERS

LIVER DISORDER	TYPE OF INJURY		RESULTS OF CHOLINE THERAPY	
	FATTY METAMORPHOSIS	NECROSIS	EXPERIMENTAL	CLINICAL
CIRRHOSIS				
Laennec's or "Alcoholic"	+++ (early)	++++ (late)	++ (early)	+ (early)
Syphilitic	±	++++	——	——
Malarial	++	++++	——	——
HEPATITIS				
Infectious	±	++++	No Exper. Infection	−(31)
Serum	±	++++		——
HEPATIC POISONING				
Phosphorous	± (early)	++++(late)	−(9)	——
Carbon Tetrachloride	± (early)	++++(late)	−(5)	+(1 case)(6)
DIETARY INJURY				
Cystine Excess	±	++++(40)	+	——
Cholesterol Excess	+++	++ (late)	±	——
Vit. E Deficiency	±	++++(46)	−	——
Choline Deficiency	++++	++ (late)	++++	——
SYSTEMIC DISEASE				
Yellow Fever	+++	++++(late)	+++(41)	——

morphosis and cellular degeneration. There appears to be some benefit in choline therapy in cases involving the first type; however, in the second type where only cell damage is involved, there is apparently no value in the administration of choline or any other lipotropic agent. It should be remembered, though, that each type is as often as not superimposed upon the other. In such cases lipotropic therapy may prove to be of considerable supplemental value. It is interesting to note that György[24] has suggested that active or supportive treatment of any general hepatic injury should consist of a proper dietary balance between methionine, cystine, and choline.

Relation to circulatory disorders. Changes produced in the liver by lipotropic imbalances evoked by various causes and acted upon in varying degrees by choline have been considered at some length. It must be realized that any changes involving the lipid metabolism of the liver must ultimately be reflected by concomitant changes in the composition of the blood and serum lipids. It is also evident that changes in serum lipids may effect other changes throughout the body.

An excellent example of this is seen in the "hemorrhagic renal syndrome" as described by Griffith.[22] As was previously mentioned, this syndrome presents a picture of subcapsular hemorrhagic lesions in combination with tubular and glomerular degeneration. A consideration of the time sequence involved in these lesions is of great importance. Griffith and Mulford[23] observed an acute onset after six to eight days on a choline-deficient diet. If the animal survived this phase until around the tenth day, the symptoms rapidly subsided and could not be reproduced even though the deficient diet was continued. At necropsy the kidneys of surviving rats showed no hemorrhage but were brown, scarred, and were covered with a "frosty" encrustation. Microscopic examination revealed interstitial tissue proliferation and gradual lysis of necrotic tissue. After several months most of the kidneys appeared normal; yet, mild chronic degeneration could be found on close examination. The reason for this amazing recovery is still in doubt; however, Griffith[22] postulates a decrease in the requirement for choline in rats over 35 days of age.

McHenry[34] feels that the cause of the "hemorrhagic renal syndrome" is a failure of phospholipids to reach the kidney through the blood, thus producing cellular failure. Another explanation of much merit lies in an answer to the question of the relation of renal damage to hypertension. In 1950 Moses, Longabaugh, and George[36] found that if rats which had survived the "hemorrhagic renal syndrome" were placed on an adequate diet, in a matter of six months they would develop severe systemic hypertension. Hartroft[26] has confirmed these findings and has done extensive work to uncover the reason for this intriguing phenomenon.

He was struck with the possibility that old latent lesions produced at the time of the acute renal episode might bear a cause-effect relationship with the resulting hypertension. He was able to demonstrate the accumulation of "fat emboli" in the capillaries of the glomeruli of the choline-deficient rats[27] which he attributed to the rupture of "fat cysts" in the liver. These emboli were consistently associated with lesions resembling Kimmelstiel-Wilson lesions of intercapillary glomerulosclerosis as seen in hypertensive diabetic man. He concluded that disturbances in fat metabolism and transport may be factors common to both choline-deficient rats and diabetic man. It was further suggested[27] that the plugging of the capillaries by the fat emboli resulted in dilation and stasis and plasma exudation (an explanation for the "hemorrhagic renal syndrome," since proteinuria but not hematuria is present.[22] This stasis is thought to be responsible for an ultimate sclerosis by permitting fibrin thrombus formation to progress in its wake. Once such a sclerosis is established, the development of systemic hypertension is a constant finding.

The dietary production of hypertension is indeed a fascinating possibility, and it is interesting to note other considerations which may have some bearing on this phenomenon. Choline-deficiency renal lesions have been found to be produced only in weanling rats, 23 to 26 days of age.[22] Arends and Nieweg[3] have reported what they consider to be a similar syndrome in human infants. They note this condition, as with the rat, is present only in young rapidly growing infants, and they propose that it may be identical with symmetrical cortical nephrosis.[51] If this is true, it would point to this syndrome as being the most common cause of renal insufficiency in infants. The implication of an association with human adult hypertension is a tempting speculation.

It follows that the exact etiology of this lesion should be determined. If it is a nutritional deficiency, as in the rat, the nature of the deficiency should be sought. In relation to this proposal, Mulford[38] found that the inclusion of vitamin B_{12} in the diet of mother rats, from birth of her litter till weaning, decreased the incidence of renal lesions in choline-deficient offspring after weaning. Choline in the mother's diet did not show a comparable effect. The significance of this finding is not at all clear; however, it helps to point up the fact that the solution of this problem can lie in any number of variables, involving not only the suckling offspring but the mother and the mother's milk as well.

In the consideration of the possibility of a relationship between dietary deficiency and systemic hypertension, one is drawn to speculate on a correlation

with associated athero- and arteriosclerosis. It has been reported[28] that atheromatous changes similar to those seen in man are noted in rats maintained on choline-deficient diets. It has also been shown that on an adequate diet the rat is refractory to these lesions.[28] Steiner,[46] however, has found that choline is capable only of delaying atheromatous changes in rabbits, although it does aid in reabsorption of the plaques. In view of these and other similar findings, Wilgram, Hartroft, and Best[50] have suggested that the term lipotropic be extended to include the prevention of fat accumulation in the heart and blood vessels as well as in the liver and kidneys.

Clinical applications of choline and other lipotropics have been made in the treatment of athero- and arteriosclerosis as well as associated hypertension and congestive heart failure. It would appear that choline alone is not effective in the prevention or cure of arteriosclerosis, for Greenberg and Bruger[21] report that no effect was observed on the concentration of blood lipids in 11 patients given 4 grams of choline per day. Goldbloom, Eiber, and Boyd[20] state that lipotropic combinations are equally ineffective on this condition. On the other hand, Abrahamson[1] reports great amelioration of symptoms and an attendant sense of well-being accompanying the administration of Methischol® (methionine, inositol, and choline) in the treatment of 86 patients with varying degrees of arteriosclerosis.

Morrison[35] is enthusiastic in his report of complete absence of deaths over a period of one year in a group of 40 patients with proved coronary arteriosclerosis and myocardial infarctions, who were treated with a combination of betaine, choline, liver fraction, and vitamin B_{12}. These results were contrasted by ten deaths in a comparable control group. He also found beneficial effects were increased by a high-protein and low-fat diet and that patients given this combined treatment showed a reduction of anginal attacks, lower susceptibility to dyspnea on exertion, ability to do more physical and mental work, a sense of well-being, and an increased appetite. It is his conclusion that lipotropic agents given in combination exert a marked synergistic effect on each other. It must be remembered, however, that with such heterogeneous mixtures, unknown factors of all sorts could be responsible for the noted effects. With this in mind, judgment of the agents reported must be reserved.

Along this same line there have been reports of choline influencing anemias in both animals and man. Davis is reported by Jukes[31] to have found choline to be related to the production of anemia in dogs; however, Jukes cites evidence indirectly showing that in man, in certain cases of macrocytic and pernicious anemia, the opposite may be true, i.e., choline may effect a cure.

In a consideration of effects on anemic states, it is perhaps worthwhile to include that it has been found[32] that choline either increases absorption of copper or limits its excretion in rats. It is known that traces of copper are essential for normal hemoglobin formation in man; this fact may, in part, explain how choline could possibly have some effect on certain anemias.

Also related to low phospholipid production and subsequent low serum phospholipid levels is a tendency toward the development of rheumatic fever. It is said[48] that resistance to this disease depends in a large degree upon serum inhibition of streptolysin-S, and that the serum inhibition depends on the level of phospholipids.

Action in Transmethylation

The relationships between the lipotropic action of choline and various bodily disorders have had many ramifications, for it is in this area of fat metabolism that most of the work to date has been done. It is evident that the process of transmethylation, as it is related to choline metabolism, can by no means be completely divorced from the lipotropic phenomenon; however, some degree of independence does appear to exist, and this problem is discussed under a separate section.

Because of the relative newness of the concept of transmethylation and the inherent difficulty in demonstrating this process experimentally, we are handicapped by having a comparatively small fund of knowledge from which to draw. In spite of this, ample evidence is available to convince one of the importance of this process. The need for labile methyl groups for the synthesis of choline and methionine has already been established. In addition, du Vigneaud[18] has shown labile methyl groups—ordinarily from methionine—are active in creatine and creatinine production as shown in Figure 2.

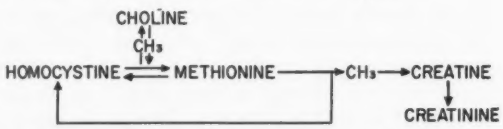

Figure 2. Transmethylation in the synthesis of creatine.[18]

Methyl groups are also required for production of epinephrine, trigonelline, cystine, and cysteine (by demethylation of methionine), N'-methyl nicotinamide, acetylcholine, as well as for certain detoxication reactions such as methylation of amines.

There can be no doubt that deficiencies of labile methyl groups will result in metabolic disturbances. It is felt[18] that pellagra may represent such a disease, since it is known that diets low in the B-vitamins are also low in choline, for choline is found naturally in conjunction with these vitamins.

The association of labile methyl groups and creatine and creatinine formation suggests a possible link between this mechanism and the experimental production of muscular dystrophy in rabbits as seen by Hove and Copeland.[30] These workers have produced characteristic lesions of muscular dystrophy by maintaining the animals on a choline-deficient diet. They found that creatine excretion was increased, while excretion of creatinine was decreased. Choline therapy brought about a rapid cure. It was established that these lesions were not due to vitamin E deficiency.

Conditions of Uncertain Relationship

An attempt has been made to correlate various metabolic phenomena with the two main physiological roles of choline, viz., its lipotropic activity and its action in transmethylation. There remain yet a few findings which defy even this broad classification, resulting from either an unexplained interplay of both actions or from some other undiscovered action.

Heller[29] has found that choline has an apparent stimulating effect on the reticulo-endothelial system. A clear interpretation of this observation is impossible at present, but in a somewhat similar vein Jukes[31] reports Chevremont as having found choline to be necessary for histiocyte formation. It may be that the application of these findings could lie in some aspect of radiation medicine, for it is well known that excessive radiation results in cellular damage.

Another interesting though puzzling action of choline is seen in its ability (in the carbamyl- form) to improve dark adaptability and produce a lowered light threshold in man.[19] It is believed that this action is due to an increased rate of regeneration of visual purple, although the nature of this process is unknown.

One final application remains to be made, viz., the high incidence of cancer in choline-deficient animals. Copeland and Salmon[14] first noted the occurrence of neoplasms in 58 per cent of animals on a choline-deficient diet over an extended period of time. No cancers were found in a similar group of control animals on an adequate diet. Since this observation, these results have been confirmed and much new information has been added. Cook and Kennaway[13] found that the sequence of choline-deficiency carcinoma closely resembled cancer produced by carcinogenic hydrocarbons. They point out that some diets reported in the literature as being used for carcinogenic studies have been deficient in choline and methionine. In addition, Maisin et al., Nakahara, Mori, and Fujiwara are reported by Cook and Kennaway[13] to have shown the presence of an "unknown anti-carcinogenic factor" in brain, liver, thymus, bone marrow, yeast, and whole rye flour. It requires but little imagination to suppose this substance might possibly be choline; however, there are many other known and probably many unknown factors in these materials, and caution should be exercised in such bold speculation. In any case, there appears to be some definite correlation between cancer and choline-deficiency. The establishment of a nutritional cause for cancer could lead to many additional advances in this field.

Summary and Conclusions

An attempt is made to review briefly the early work from which evolved the nature, physiological importance, and metabolic functions of choline. For purposes of discussion, experimental findings are arbitrarily divided into those involving the lipotropic activity of choline and those related to its action in transmethylation. Some diseases of man are correlated with these activities, in order to assess the value of actual or theoretical therapeutic applications of choline in the treatment of these diseases.

It is concluded that:

1. Choline is a valuable supplemental therapeutic agent in the treatment of general hepatic injury, especially in conditions involving extensive fatty infiltration of the liver.

2. Choline is of little or no value in the treatment of conditions involving extensive degenerative necrosis of liver cells.

3. A relationship may exist between infant choline deficiency and adult systemic hypertension.

4. Choline in combination with other lipotropic agents is moderately effective in the relief of symptoms and in the production of general improvement in some cases of arteriosclerosis and related circulatory disorders.

5. The effects of choline on the reticulo-endothelial system, the visual purple of the eye, and in the prevention of certain types of experimental cancer, seem to indicate unexplained facets still exist in the metabolism of choline.

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Federal Tax Information

A film on federal taxes, "Clinic on Federal Finances," has been made by the Tax Foundation, 30 Rockefeller Plaza, New York 20, New York, and is available for showing to taxpayer, farm, employee, and other groups under local sponsorship.

It tells a story in charts, tables, and quotations from national fiscal leaders about the growth of U. S. expenditures, the problem of controlling debt and inflation, and the present tax burden. The film, in color, runs about 30 minutes.

Official Proceedings

Report of Two Meetings of the House of Delegates, May 7, 1957 and May 9, 1957

First Meeting

The first 1957 meeting of the House of Delegates of the Kansas Medical Society was held on Tuesday morning, May 7, at the Allis Hotel, Wichita, following a 7:30 breakfast. Dr. Clyde W. Miller, Wichita, president, presided.

The presence of a quorum was announced by Dr. A. W. Fegtly, Wichita, sergeant at arms, who reported the attendance of 72 delegates, 3 past presidents, 7 officers, 12 councilors, and 6 guests.

Dr. Miller introduced and thanked Dr. William J. Reals, Dr. Norton L. Francis, and Dr. E. S. Brinton, all of Wichita, for their service in summarizing the reports of officers, councilors, and committee chairmen. Dr. Reals, as chairman of the group, introduced 30 resolutions from the reports, all of which were scheduled for action at the second meeting of the House.

Dr. Orville R. Clark, Topeka, chairman of the Editorial Board, gave his annual report. In the absence of the treasurer, Dr. John L. Lattimore, Topeka, Mr. Oliver E. Ebel, executive secretary, presented figures from a preliminary audit for the fiscal year ending April 30, 1957.

Dr. Cyril V. Black, Pratt, state chairman of A.M.E.F., presented an award to Dr. John F. Thurlow, Hays, for a large individual contribution and a certificate of merit to the Society, which ranked 12th among all state organizations with reference to A.M.E.F. gifts.

Six resolutions were introduced for consideration at the second meeting of the House.

Announcements by the president concluded the meeting.

Second Meeting

The second 1957 meeting of the House of Delegates of the Kansas Medical Society was held at the Allis Hotel, Wichita, after a 12:30 luncheon on Thursday, May 9.

The president, Dr. Clyde W. Miller, Wichita, began the meeting by calling on Dr. A. W. Fegtly, Wichita, sergeant at arms, for a report on attendance. Dr. Fegtly reported the registration of 72 delegates, 6 officers, 4 past presidents, 9 councilors, and 4 visitors.

The president then introduced Dr. George L. Thorpe, Wichita, who had served as chairman of the Reference Committee which considered all business introduced at the first meeting of the House. Also on the committee were Dr. Clarence H. Benage, Pittsburg; Dr. Glenn R. Peters, Kansas City; Dr. Lloyd W. Reynolds, Hays, and Dr. Frederick E. Wrightman, Sabetha.

Dr. Thorpe, reporting for his committee, recommended referring to the Council for approval the request of the councilor from District 15 for issuance of a charter to combine physicians in Comanche, Kiowa, Clark, and Meade counties into a component organization of the Kansas Medical Society to be know as the Iroquois Medical Society. The House concurred.

Also approved by the House, on recommendation of the Reference Committee, were reports from the following committees: Allied Groups, Auxiliary, Blue Shield Fee Schedules, Blue Shield Relations, Centennial, Child Welfare, Conservation of Eyesight, Conservation of Hearing and Speech, Control of Cancer, Control of Tuberculosis, Emergency Medical Care, Endowment, General Practice Award, History, Hospital Survey, Industrial Medicine, Maternal Welfare, Medical Assistants, Medical Economics, Medical Practice Act, Medical Schools, Mental Health, Pathology, Postgraduate Study, Public Relations, Rural Health, Safety, Stormont Medical Library, and Study of Heart Disease.

Next reported were two recommendations of the Committee on Constitution and Rules which were unanimously approved: 1) that small county societies merge with neighboring small county societies to form multi-county societies of more than 20 members, and (2) that charters be issued to such newly formed multi-county societies and that replacement charters be issued to existing groups which do not now have their original charters.

A third recommendation of the Committee on Constitution and Rules, that invitations to make annual reports to the House of Delegates be extended to the presidents of such groups as the Woman's Auxiliary to the Kansas Medical Society, the Kansas Medical Assistants' Society, and Blue Shield, to the chairman of the Kansas State Board of Medical Registration and Examination, and to the dean of the University of Kansas School of Medicine, was approved with the addition of the word "MAY." This provides that such invitations MAY be issued.

Eleven amendments to the by-laws of the Society were approved with the following wording:

AMENDMENT NO. 1

By-Laws, Chapter V, Section 8.—The agenda revised to read:

1. Registration of Delegates, ex-officio members and visitors.
2. Call to order by the President.
3. Announcement of number of Delegates, ex-officio members present and registered and the presence of an official quorum.
4. Reading of the minutes of last and any special meeting.
5. Report of Reference Committee on reports printed in the JOURNAL with details of recommendations and resolutions therein requiring action by the Society.
6. Supplemental reports from committees or officers.
7. Report of Executive Secretary.
8. Report of the Treasurer.
9. Unfinished business.
10. New business and resolutions offered.
11. Address of the President (if desired).
12. Address of the President-Elect (if desired).
13. Announcements—to include time and place of Reference Committee meeting.
14. Adjournment to reconvene at second meeting.

AMENDMENT NO. 2

By-Laws, Chapter XI, Section 1a. Amend as follows:

Delete Committee of Advisory Past Presidents	Sec. 35
Delete Committee on Venereal Diseases	Sec. 34
Change name of Committee on Hospital Survey to Committee on Hospitals .	Sec. 21
Include Committee on Anesthesiology .	Sec. 38
Include Committee on Gerontology . .	Sec. 39
Include Committee on Safety . . .	Sec. 40

AMENDMENT NO. 3

By-Laws, Chapter XI, Section 1b. Amend to read:

Special Reference Committee on Reports printed in the JOURNAL.

Special Reference Committees on Recommendations and Resolutions.

AMENDMENT NO. 4

By-Laws, Chapter XI, Section 3, Paragraph 1:

(a) Line 1, delete word "special" and remove parentheses from word "temporary."

By-Laws, Chapter XI, Section 3, Paragraph 2. Amend to read:

(b) Special Reference Committee on Reports printed in the JOURNAL, to consist of two or more members, shall be appointed at least 30 days before each annual session. Their duties shall be to review all reports printed in the JOURNAL and prepare written report giving in detail each recommendation or resolution proposed which requires approval or disapproval of the House of Delegates. Their report merely establishes that these matters require action by the House of Delegates, and may recommend that the reports AS PRINTED, with the exception of the specific items given, be approved as published.

(c) The Special Reference Committees on Recommendations and Resolutions, to consist of five or more, shall be appointed at each annual session. They shall meet at a designated time and place between the sessions of the House of Delegates for consideration of all recommendations and resolutions presented to the House of Delegates requiring specific action or policy of the state Society after public hearings on the same. They shall report, complete with recommendation for approval, disapproval, or adoption, in writing, their conclusions on each subject to the second or last meeting of the House of Delegates.

(d) By-Laws, Chapter XI, Section 3, Paragraph 3. Shall be deleted.

AMENDMENT NO. 5

By-Laws, Chapter V, Section 19. House of Delegates. Amend by the addition of paragraph to be No. 1:

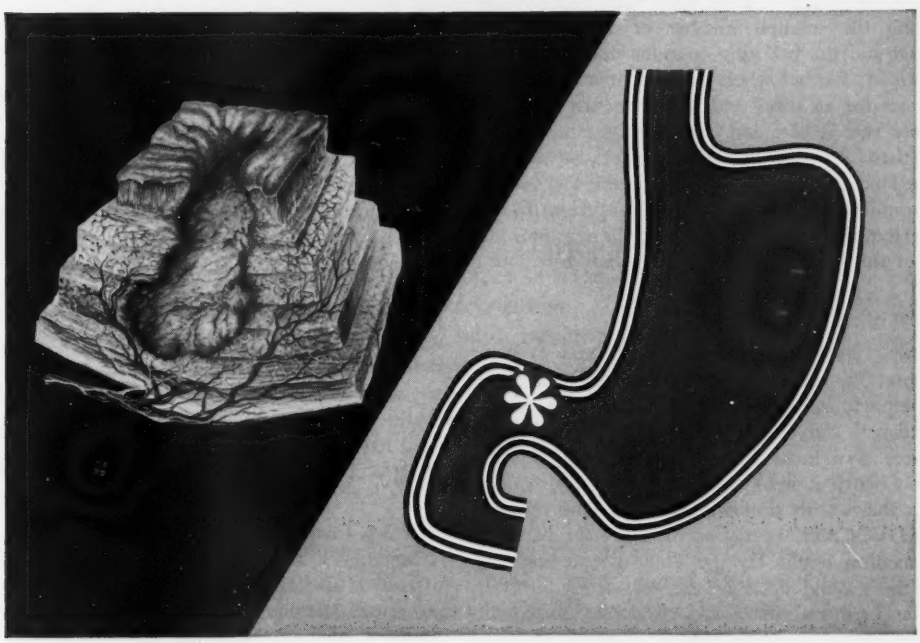
a. Section 19: All reports and resolutions for consideration of the House of Delegates to be published in advance of the annual session shall be sent to the executive office at least six weeks before the date of the annual session. Any supplementary reports or resolutions by individual members or component societies, to be acted upon by the House of Delegates, and not sent in time for publication, shall be written and three copies shall be sent to the Executive Office not less than five days before the annual session.

b. Permission is requested upon the reprinting of the By-Laws to include in duties of Defense and Editorial Boards and certain officers where it has been omitted:
"Written report shall be made annually to the House of Delegates."

AMENDMENT NO. 6

By-Laws, Chapter VI, Section 3. Election of Officers. Shall be amended to read:

BROAD ANTICHOLINERGIC BLOCKADE



Pro-Banthine® Relieves Pain, Accelerates Peptic Ulcer Healing

The efficiency of Pro-Banthine (brand of propantheline bromide) in inhibiting the chemical substance which mediates parasympathetic gastric activity explains the success of the drug in ulcer therapy. Pro-Banthine blocks acetylcholine at both the ganglia and parasympathetic effector sites. This dual action controls excess neural stimulation of both gastric secretion and motility.

The therapeutic benefits of this anticholinergic blockade consist, as many clinical investigators have noted, in prompt relief of ulcer pain and pronounced acceleration of ulcer healing.

The suggested initial dosage is one 15-mg. tablet with meals and two tablets at bedtime. Two or more tablets four times a day may be indicated in severe manifestations. G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.

SEARLE

Section 3. All elections of officers shall be by secret ballot unless a single candidate is nominated for office, whereupon the vote may be given viva voce. If upon any ballot for three nominees no nominee shall receive a majority vote, the nominee receiving the smallest number of votes shall be dropped and the balloting continue until a majority is obtained: Further when there are more than three nominees for an office and upon the first ballot no majority vote is obtained, all candidates having less votes than any one of the highest three shall be dropped and voting continue as outlined above for three candidates. Nominations for all offices may be made from the floor in addition to the recommendations of the Nominating Committee before balloting begins.

Amendment No. 7

By-Laws, Chapter XI, Section 30. Amend to read:

Section 30. The Committee on Public Policy shall be composed of the Executive Committee of the Council, all active Past-Presidents, and such other members as deemed advisable. Under the direction of the Council it shall represent the Society in keeping in touch with professional and public opinions and ADVOCATE legislation to secure the best possible medical results for the whole people and promote the general good of the community in local, state, and national affairs and elections. Sub-committees for special purposes may be formed. Meetings shall be held at the call of the President.

Amendment No. 8

By-Laws, Chapter XI, Section 38. Shall read:

The Committee on Anesthesiology shall consist of at least five members. It shall be the function of this committee to stimulate interest among anesthetists both full time and part time in preparing papers for publication; to study post-surgical deaths in the hospitals of the state; to encourage all anesthesiologists to participate fully in all component society meetings, with emphasis on improving the safeguards to patients requiring anesthesia, and to co-operate in furthering the purposes and the meetings of the Kansas Society of Anesthesiologists. Meetings shall be called by the chairman. At least one-half of the membership shall have served on the retiring committee.

Amendment No. 9

By-Laws, Chapter XI, Section 39. Shall read:

Section 39. The Committee on Gerontology shall be composed of five or more members appointed by the President. Its purpose shall be to study the medical, social and economic aspects of gerontology. They shall also study methods of establishing, controlling, licensing, and improving nursing homes for the care of the aged. They shall endeavor to assist and co-operate with such departments of state government whose business it is to supervise such homes. They shall meet at the call of the Chairman. At least one-half the membership shall have served on the retiring committee.

Amendment No. 10

By-Laws, Chapter XI, Section 21. Amend to read:

Section 21. The Committee on Hospitals shall consist of five or more members, one of whom shall be the member serving on the Kansas Hospital Advisory Commission. The duties of this committee shall be to consider the problems of the hospitals of the state, co-operate with the Hospital Committee of the American Medical Association, the Kansas Hospital Advisory Commission, and the Joint Commission on Accreditation, and endeavor to secure proper rating and accreditation of hospitals and satisfactory physician-hospital relations. Meetings shall be called by the Chairman. At least one-half the membership shall have served on the retiring committee.

Amendment No. 11

By-Laws, Chapter XI, Section 40. Shall read:

Section 40. The Committee on Safety shall consist of at least five members. It shall be the duty of this committee to study the medical aspects of safety programs of all agencies, public and private, to coordinate similar studies from all sources, and to recommend and initiate such action as may be deemed necessary, advantageous, and proper for the members of the Society. At least one-half of the committee membership, one of whom is the retiring chairman, shall have served on the retiring committee. Meetings shall be called by the Chairman.

Dr. Orville R. Clark, chairman of the Committee on Necrology, read a list of Society members whose deaths were reported during the course of the past year and asked a moment of silence as a tribute to those physicians.

Dr. Thorpe next presented a resolution prepared by his committee after a review of the request of the Committee on School Health. The resolution provided that the executive secretary inform each component society by letter that it consider the appointment of a Committee on School Health in an effort to solve local problems and in addition to cooperate with the state committee and coordinate the state program. The resolution was approved.

Noting that a resolution to discontinue the Committee on Venereal Disease was included in the report of the Committee on Constitution and Rules (Amendment No. 2), Dr. Thorpe's committee recommended that the report of the Committee on Venereal Disease be tabled. The House voted to do so.

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A Better Antihypertensive

. . . because among all Rauwolfia preparations Rauwiloid (alseroxylon) is maximally effective and maximally safe . . . because least dosage adjustment is necessary . . . because the incidence of depression is less . . . because up to 80% of patients with mild labile hypertension and many with more severe forms respond to Rauwiloid alone.

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Dosage: Simply two 2 mg. tablets at bedtime. After full effect one tablet suffices.

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Rauwiloid is recognized as basal medication in all grades and types of hypertension. In combination with more potent agents it proves synergistic or potentiating, making smaller dosage effective and freer from side actions.

Rauwiloid®+Veriloid®

In moderate to severe hypertension this single-tablet combination permits long-term therapy with dependably stable response. Each tablet contains 1 mg. Rauwiloid and 3 mg. Veriloid. Initial dose, 1 tablet t.i.d., p.c.

Rauwiloid®+ Hexamethonium

In severe, otherwise intractable hypertension this single-tablet combination provides smoother, less erratic response to hexamethonium. Each tablet contains 1 mg. Rauwiloid and 250 mg. hexamethonium chloride dihydrate. Initial dose, ½ tablet q.i.d.

Riker LOS ANGELES

On Dr. Thorpe's recommendation, unanimous approval was given the reports of the president of Blue Shield and the chairmen of the Committee on Dues and Hardships and the Committee on Medicare Program.

A supplementary report of the Committee on Medical Economics was next discussed. Dr. Thorpe reported his committee's recommendations as follows: that the committee be commended; that the committee obtain the broadest possible insurance coverage in a reliable company at the lowest available cost; that existing agreements with insurance carriers be terminated if improved terms can be obtained through another carrier, only after the existing carrier has been invited to meet with the Committee on Medical Economics upon the termination procedure and if there is complete assurance that no member currently insured can lose his insurance benefits because of such change. The House accepted the recommendations.

Also accepted by the House was a special report of the Committee on Relations with the Bar Association. The House acted to refer three items requiring action to the Committee on Allied Groups for implementation and adoption with the approval of the Council. The three items provide for (1) ultimate adoption of an inter-professional code of ethics between doctors and lawyers; (2) participation by doctors and lawyers in a panel discussion on inter-professional relationships at the 1958 meeting of the Kansas Medical Society, and (3) provision of speakers on the subject of inter-professional relationships for local medical societies.

The House accepted a report of the Kansas State Advisory Committee and thanked members of the committee for their services.

On the recommendation of Dr. Thorpe, the House voted thanks to members of the Shawnee County Medical Society who rendered professional services to legislators during the 1957 session of the Kansas legislature.

To carry out the recommendation of the Committee on Constitution and Rules that multi-county societies be formed, the House approved Dr. Thorpe's plan that the executive secretary prepare a report of all component societies, listing their geographical boundaries and their membership, and submit such information to the Council by October so that negotiations for the formation of multi-county societies may be begun.

Medical care for the indigent was briefly discussed. It was the recommendation of Dr. Thorpe's committee that each county society negotiate its own contract, and this view prevailed when the House voted.

Referred to the Committee on Blue Shield Relations, on a motion by Dr. Thorpe, was the matter of establishing closer relations between the Society and Blue Shield.

Also in accordance with a motion by Dr. Thorpe, the House recommended that the president, with the consent of the Council, appoint a Special Committee on Federal Legislation to provide more information on this subject to the membership.

Dr. Thorpe next reported his committee's approval of a suggestion that a special committee be appointed to meet with representatives of other professions to work out problems that may arise from the new Medical Practice Act, and that this committee be made answerable to the Council. The House voted its approval.

The report of the constitutional secretary was then unanimously approved.

In accepting the report of the senior delegate to the A.M.A. from Kansas, Dr. Laurence S. Nelson, Sr., Salina, the House adopted a resolution praising his ability and service and directed that a letter of commendation be written him by the executive secretary. The report of the second delegate, Dr. George Gsell, Wichita, was also accepted with appreciation.

In considering the report of the president, the House accepted Dr. Thorpe's recommendations on the following points: (1) that a Kansas room be maintained for the entertainment of Kansas physicians and delegates from other states at meetings of the A.M.A.; (2) that the Committee on Medicare be continued with instructions to report to the Council on all changes and threats of changes; (3) that the Society not endorse any plan regarding polio vaccine until such time as the polio immunization program is stabilized; (4) that a vote of thanks be tendered to office employees, and (5) that it be recommended to the Council that annual Society dues for 1958 be set at $50 per member.

The report of the president-elect, Dr. Barrett A. Nelson, Manhattan, was approved by the House. Special consideration was given his suggestion that mental health receive marked study, and the House voted to refer this study to the Committee on Mental Health with instructions that it secure Council approval for implementing the programs required. A resolution of support for Dr. Nelson's program for the coming year was passed unanimously.

Dr. Thorpe, in telling of his committee's action, asked and received approval of the report of the president of the Woman's Auxiliary to the Kansas Medical Society, Mrs. William J. Biermann, Wichita, and suggested that the report be printed in the JOURNAL. (Editor's Note. See June issue, Page 387).

The report of the executive secretary of the Kansas State Board of Health, Dr. Thomas R. Hood, was approved with an addition. The House appended to the list of bills of interest to public health workers

Meat...

and Protection Against Hypochromic Anemia

Hypochromic anemia, the most common nutritional deficiency in children in the United States, occurs most frequently in the second six months after birth.[1] A major cause of anemia in early infancy may arise from insufficient transfer of iron from the mother to the fetus,[2] since anemia is not uncommon in pregnant women.

A first step, then, toward prevention of hypochromic anemia in the infant is the provision of a prenatal diet rich in available iron and in high quality protein. A second and most important step is the addition of foods high in utilizable iron (egg yolk, sieved meat and vegetables) to the infant's daily diet as early as possible (usually 3 months after birth).[1]

Meat contributes valuable amounts of anabolically effective protein, B vitamins, readily available iron, and other minerals to the nutrition of the pregnant and lactating woman. The feeding of sieved meat to infants after the third month provides well-utilized iron and aids in the prevention of hypochromic anemia.

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1. Jackson, P. L.: Iron Deficiency Anemia in Infants, Editorial, J.A.M.A. *160*:976 (Mar. 17) 1956.

2. Martin, E. A.: Roberts' Nutrition Work with Children, Chicago, The University of Chicago Press, 1954, p. 211.

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

American Meat Institute
Main Office, Chicago...Members Throughout the United States

as enacted in the 1957 session of the Kansas legislature, House Bill No. 130, providing for a hospital in Northeast Johnson County, subject to the will of the people.

Also approved was the report of the Kansas State Board of Medical Registration and Examination, and commendation was given by the House to members of that board.

Next on the agenda for the House of Delegates was consideration of the six resolutions introduced at the first meeting under the heading of new business. On the recommendation of Dr. Thorpe and his committee, the following resolution introduced by Dr. Glen R. Floyd, Winfield, was approved:

WHEREAS, We the members of the Ophthalmology Section of the Kansas Medical Society have seriously studied and considered, with reference to the welfare of the public as a whole, the announcement of the American Board of Ophthalmology of its intent to establish a certification in ophthalmic surgery; and

WHEREAS, It is fundamentally the purpose and responsibility of the American Board of Ophthalmology in certifying candidates, to guarantee to the public that the certified ophthalmologist is qualified in all phases of ophthalmology and competent to assume his responsibilities in that branch of medical practice; now, therefore be it

Resolved, that it is our considered judgment that surgical certification apart from the certification in Ophthalmology has not been demonstrated to be in the interest of the public or of the profession and should not be offered for the following reasons:

1. Ophthalmic surgery is a therapeutic procedure within the practice of ophthalmology and does not constitute the basis for the establishment of a separate specialty or subspecialty.

2. If, in the opinion of some members of the Board, the competency of some diplomates is in doubt, it is the obligation of the Board to review its methods of examination and criteria for qualification, since the failure to do so would subject our Board to severe censure, and would evaluate the status of its certificate. In this regard, the acceptance of this new Board of Ophthalmic Surgery would effectively decertify all diplomates who now possess the certificate from the Board of Ophthalmology.

3. Certification by the Board is only one of the regulating mechanisms operating in medicine for the protection of the public. Certification has not given or assured prompt acceptance to the staff of any hospital. Each individual has generally been required to prove his competency before his associates at the local level. This local regulation has now been made mandatory in order that hospital officials maintain accreditation from a Commission composed of responsible members of the American College of Surgeons, American College of Physicians, American Hospital Association and the American Medical Association.

4. Medical Liability Insurance has become an important consideration in modern medical practice. To downgrade the innumerable competent ophthalmologists who have demonstrated their surgical ability over the years might conceivably destroy the public confidence, particularly in the smaller community, and subject such men to unjustified harassment.

5. Special recognition as an ophthalmic surgeon is already available through the American College of Surgeons, (revised qualifications) where, in addition to the listing of a large number of cases and submission of case reports, one is required to perform in his own community situation before a reviewing authority composed of recognized competent ophthalmic surgeons.

6. A change in policy of such sweeping consequences should be effected only after discussion with and consideration by all diplomates concerned.

A second resolution offered by Dr. Floyd was also approved as follows:

WHEREAS, There has been presented a Resolution, passed by the Ophthalmology Section of the Kansas Medical Society relative to the proposed establishment of a special certification by the American Board of Ophthalmology in ophthalmic surgery; and

WHEREAS, The Resolution adopted by the Ophthalmology Section of the Kansas Medical Society, a copy of which is attached hereto and made a part hereof, has been presented to this group for consideration, approval and action; and

WHEREAS, Said Resolution of the Ophthalmology Section has been given due study and consideration; and

WHEREAS, It is deemed that the position of the Ophthalmology Section is well taken; now, therefore be it

Resolved that the Resolution of the Ophthalmology Section of the Kansas Medical Society, a copy of which is attached hereto and made a part thereof, be accepted and approved. Be it further

Resolved that copies of this Resolution shall be sent to all members of the American Board of Ophthalmology, to the various state and local ophthalmological organizations, to all state medical societies, to the Section on Ophthalmology of the American Medical Association and to the American Academy of Ophthalmology and Otolaryngology.

A resolution on life insurance introduced at the first meeting of the House by Dr. Laurence S. Nelson, Jr., Salina, was approved as follows:

WHEREAS, The House of Delegates at the recommendation of the Committee on Medical Economics

Youngsters really go for the taste-true orange flavor of ACHROMYCIN V SYRUP. But this new syrup offers more than "lip-service" to your junior patients. It provides the new benefits of RAPID-ACTING, phosphate-buffered ACHROMYCIN V—

a faster-acting oral form

- accelerated absorption in the gastrointestinal tract
- earlier, higher peaks of concentration in body tissue and fluid
- quicker control of a wide variety of infections
- unsurpassed true broad-spectrum action
- minimal side effects
- well-tolerated by patients of all ages

ACHROMYCIN V SYRUP: aqueous, ready-to-use, freely miscible. 125 mg. tetracycline per 5 cc. teaspoonful phosphate-buffered.

DOSAGE: 6-7 mg. per lb. of body weight per day.

*Reg. U. S. Pat. Off.

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

on May 3, 1956, approved a group life insurance plan for physicians of Kansas, and

WHEREAS, Not less than six membership letters have been sent to the membership outlining the program, and

WHEREAS, In order to put the program into effect 60 per cent of the membership or 500 members need to enroll and at the present time 250 members have applied, and

WHEREAS, Representatives of the American United Life Insurance Company are present, exhibiting at this meeting, therefore be it

Resolved, that members of the House of Delegates make every effort, at this meeting and at home, to inform the physicians of this opportunity for life insurance. Be it further

Resolved, that the time limit for enrollment be extended to June 15, 1957, and if the needed number of physicians have not applied for insurance by that date the program be cancelled and the problem referred to the Committee on Medical Economics for further study.

A resolution introduced by Dr. H. P. Jubelt, Manhattan, at the first meeting of the House was next reported by Dr. Thorpe. He said his committee approved the intent of the resolution, that different specialties of medicine be represented on the committee planning the program for each state meeting. The committee felt that the objective could be realized by directing the executive secretary to invite each specialty society to recommend a speaker for the state meeting and to submit the names of speakers so recommended to the program committee in the city in which the meeting is to be held. The House voted to follow that plan.

Also approved by the House was a resolution by Dr. Max Lake, Salina, providing for publication of an alphabetical and geographical list of members of the Kansas Medical Society, the exact contents to be decided by the Council.

The final resolution, submitted by Dr. Karl Voldeng, Wellington, for the South Central Tri-County Medical Society, related to the lack of a uniform plan for contracting for medical care of the indigent in Kansas and suggested a study of past expenditures for this purpose. Dr. Thorpe reported his committee's sympathy with the objectives of the resolution and belief in the futility of carrying out such a study. For that reason he recommended that the resolution not be passed, and the House followed his suggestion.

In concluding his part of the meeting, Dr. Thorpe thanked all who had helped the committee.

Dr. Wrightman, upon receipt of permission to introduce a resolution, asked for and received a standing vote of appreciation to Dr. Miller for his many services to the Society during his year as president.

After miscellaneous announcements, ballots were distributed for the election of officers. Dr. Orville R. Clark, Topeka, who had been one of those nominated for the office of second-vice president, asked that he not be considered for the position, and his name was withdrawn. No nominations were made from the floor, and officers were elected as reported in the June issue of the JOURNAL. Representatives of the councilor districts scheduled for the appointment of new councilors this year then reported the names of those chosen. In the final balloting five past presidents were elected to serve as members of next year's Nominating Committee, as reported in the June issue of the JOURNAL.

In accordance with a motion by Dr. Oscar W. Davidson, Kansas City, the House unanimously passed a recommendation to the Council that Dr. Orville R. Clark, Topeka, be retained as editor of the JOURNAL.

By another unanimous vote, the House expressed appreciation to the Sedgwick County Medical Society for an excellent meeting and for its hospitality.

Dr. Miller expressed thanks to the members of the two reference committees, after which he asked for suggestions for improving the format of state meetings. Several suggestions were made.

Dr. Miller then turned the gavel over to Dr. Nelson, the new president, who spoke briefly and concluded the meeting with announcement of next year's session in Kansas City.

Speeding on U. S. streets and highways last year killed 12,700 men, women, and children.

DEATH NOTICES

EARL FINLEY CLARK, M.D.

Dr. Earl F. Clark, 77, an honorary member and past president of the Tri-County Medical Society, died at the Veterans Administration Hospital in Wichita on June 2. A graduate of the University of Kansas School of Medicine, he had practiced first in Mayfield. During World War I he served in the Medical Corps of the Army, after which he did postgraduate work in ophthalmology at the University of Illinois. He began practice in Belle Plaine in 1922 and continued in practice there until his death. He had served one term as commander of the American Legion post in Belle Plaine, and in 1927 he served as a delegate to the Legion convention in Paris.

among nonhormonal antiarthritics...
unexcelled in
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In the nonhormonal treatment of arthritis and allied disorders no agent surpasses BUTAZOLIDIN in potency of action.

Its well-established advantages include remarkably prompt action, broad scope of usefulness, and no tendency to development of drug tolerance. Being nonhormonal, BUTAZOLIDIN causes no upset of normal endocrine balance.

BUTAZOLIDIN relieves pain, improves function, resolves inflammation in:
Gouty Arthritis
Rheumatoid Arthritis
Rheumatoid Spondylitis
Painful Shoulder Syndrome

BUTAZOLIDIN being a potent therapeutic agent, physicians unfamiliar with its use are urged to send for detailed literature before instituting therapy.

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Ardsley, New York

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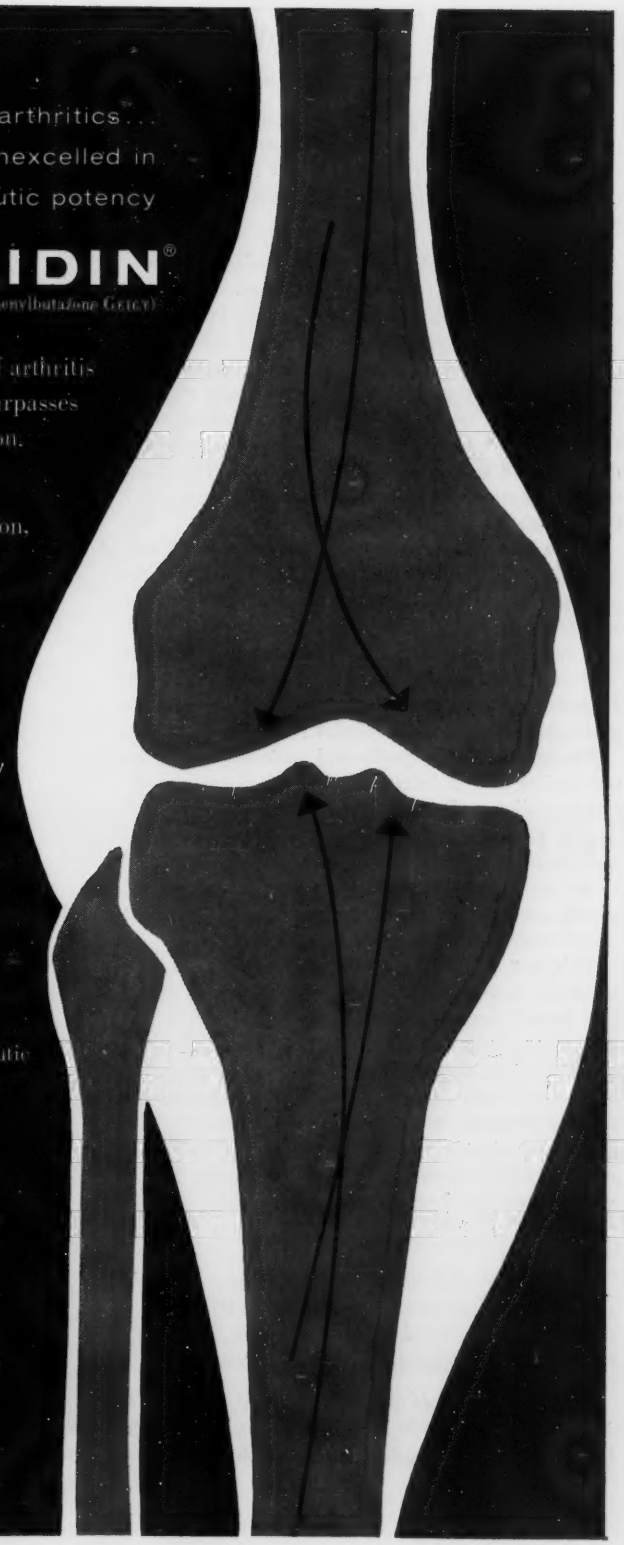

BOOK REVIEWS

Principles of Urology—An Introductory Textbook to the Diseases of the Urogenital Tract. By Meredith F. Campbell, M.D. Published by W. B. Saunders Company, Philadelphia. 622 pages, 319 figures. Price $9.50.

Dr. Meredith F. Campbell has produced an excellent first edition textbook on urology. The introduction, or Chapter I, is treated unusually by presenting a complete glossary of urological terms and definitions. It makes a study of the following chapters more easily understandable by the neophyte student.

The chapter on history-taking and examination is forcefully and clearly presented. X-ray studies are excellent and well-fitted into the diagnosis. The chapter on anatomy could be strengthened by more illustrations and annotations.

There is a splendid chapter on embryology and anomalies, but probably more detailed than the medical student needs. I like the treatment on infections and feel it is invaluable to the general practitioner and surgeon who is not a urological specialist, as well as the student. Again the treatment of the male reproductive tract could be very satisfactory for the undergraduate and truly helpful for the practitioner.

Neuro-muscular uropathy and acute trauma of the uro-genital tract is interesting and adequate. Urinary calculus disease is well discussed. The section on tumors presents thorough differential diagnosis and indications for treatment of choice. One is treated to an extra premium with a chapter on the adrenal glands and diseases. It is perhaps one of the most meaty chapters in the whole book.

This text has left out unlikely theories and controversial material and descriptions of major operative procedures. The book commends itself to the medical faculties for their text in urology and to the general practitioner or general surgeon for improvement or refreshment on the subject of urology. An unusual inclusion is a chapter of questions with page references to permit the student to examine himself on the subject covered or to help him prepare for the various state board examinations.—*G.E.K.*

A Textbook of Histology. By Alexander A. Maximow and William Bloom. Published by W. B. Saunders Company, Philadelphia. 628 pages, 1082 illustrations, 265 in color on 631 figures. Price $11.

The first edition of this excellent text appeared in 1930 shortly after its senior author's death. The translation of the chapters dealing with the nervous system in the Russian text of 1918 and extensive notes (English), especially on blood and blood-forming organs, along with those on connective tissue, formed the nucleus upon which Professor Maximow's colleagues at the University of Chicago relied in the completion of the book. Professor William Bloom has from the first been the chief author and editor, contributing chiefly the material on the biliary and respiratory systems, pancreas, and endocrine glands. Contributors and assistants are too numerous to mention in the continued editions of this exceptional treatise on the finer detailed microscopic anatomy of the human body. This phase is what makes this classic so popular.

Maximow insisted that wherever possible human material should be used. Each successive edition has maintained this, but new techniques have permitted an ever improved approach to the ultra fine structure of the human tissues, to the point where many electron micrographs enable the medical man to grasp the deeper significance of the submicroscopic world. These new vistas permit a greater understanding to the point where histology, biochemistry, and biophysics are fused into an exciting insight into nature's secrets.

Some portion of all systems of the vertebrate body has been illustrated by electron micrographs with exceptional fidelity.

As in the past, the present edition contains useful summaries of each system which deal with histogenesis and histophysiological principles. There appear here also pertinent references to recent literature.—*P.G.R.*

The Ciba Collection of Medical Illustrations, Volume III. Digestive System, Part III, Liver, Biliary Tract, and Pancreas. By Frank H. Netter, M.D. Commissioned and Published by Ciba Pharmaceutical Products, Inc. Price $13.

As indicated in the title, this is Part III of a series devoted to the gastrointestinal tract. Parts I and II will follow at a later date. Utilizing to the greatest advantages the long recognized talents of Dr. Netter and complementing this with contributions of a distinguished consulting staff, the publishers have produced an amazingly lucid and useful volume.

A section illustrating and discussing anatomy of the liver, biliary tract, and pancreas is followed by sections on normal and disturbed physiology, diseases of the liver, diseases of the gallbladder and bile ducts and, finally, a section describing by illustration and text diseases of the pancreas.

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Marquis, D. G., Kelly, E. L., Miller, J. G., Gerard, R. W. and Rapoport, A.: Ann. New York Acad. Sc. 67:701, May 9, 1957.

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Keyes, B. L.: Pennsylvania M. J. 60:177, Feb. 1957.

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Sokoloff, O. J.: A.M.A. Arch. Dermat. & Syph. 74:393, Oct. 1956.

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Kessler, L. N. and Barnard, R. D.: M. Times 84:431, April 1956.

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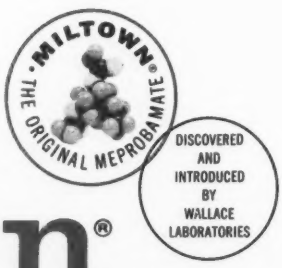
Rindskopf, W., Ravreby, M., Gutenkauf, C. and Sands, S. L.: J. Iowa M. Soc. 47:57, Feb. 1957.



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clear manner the most recent concepts of liver structure. Liver function and the "metabolic pool" are subsections so vividly and imaginatively depicted as to make much more easily understood many of the biochemist's concepts of liver activity.

All clinicians and surgeons, as well as others, will find each section—liver, biliary tract and pancreas—presenting the subject with new clarity. The text is of necessity concise and compressed, but an excellent bibliography offers quick access to an extensive literature.—*M.H.D.*

Battle for the Mind. By William Sargant. Published by Doubleday and Company, Inc., New York. 263 pages. Price $4.50.

The common denominators of various "mind influencing" techniques are looked for by Dr. Sargant in the Pavlovian concepts of conditioned reflexes, and the effects of their disruption. Personal observations, as well as those of colleagues in World War II, contemporary historical accounts of religious conversion experiences, psychiatric treatment, both of psychotherapy and physical therapies, "brain washing" techniques, and Pavlov's animal experiments are all examined to provide data and evidence for his basic thesis.

In summary form this is that man integrates expressions, concepts, or beliefs from his environment into his behavioral and thought reflexes. The changing or alteration of these, by whatever techniques or for whatever purpose, follows a definite pattern. First strong emotional responses are aroused in some form such as tension, fears, anxiety, guilt, religious frenzy or frustration of instinctual drives which may be further accentuated by physical factors such as exhaustion. When the nervous system has been stimulated beyond its capacity to respond normally ("transmarginally"), inhibition occurs which is protective and results in altered behavior. In human thought and behavior this would result in uncertainty, in which suggestibility is increased and old behavior and thought patterns are disrupted and new concepts or beliefs can be imposed. Consideration is given to response to stress situations varying in accordance with different types of inherited temperament, as well as different patterns of response to transmarginal stimulation and inhibition.

It is felt that Dr. Sargant has made a scientific effort to bring together and explain what has been considered by many as separate or drastically different areas of human thought and behavior. The book already has been criticized or rejected by those who feel an evaluation or comparison is being made between their discipline or tenets and something seemingly diametrically opposed to it. Wesley's religious conversions are discussed along with voodoo and snake handling cults, even though Dr. Sargant makes no value judgments of the examples he chooses; he is concerned only in the modus operandi that makes possible any alteration in belief or behavior. Similar resentment could well come from his seeking common factors in psychoanalytic treatment and electro-convulsive therapy for mental illness; or in what might erroneously be misinterpreted as a comparison between Communistic brain washing methods and humanitarian reform movements.

If the study can be viewed scientifically, however, it is interesting and provocative reading, not only for the examples chosen but the ease with which extensions of the thesis expressed can be applied to the reader's own particular field of interest.—*J.D.*

The Riddle of Stuttering. By C. S. Bluemel, M. D. Published by Interstate Printers and Publishers, Inc. Danville, Ill. 142 pages. Price: Hard bound, $3.50; Paper bound, $1.50; Therapy Records, $3.00.

This excellent book deals with therapy as much as with theory, and it should prove useful to the family doctor, the pediatrician, the psychiatrist, the speech correctionist, and the adult stutterer. Four 12-inch long-play speech therapy recordings are available. All proceeds from the sale of these books and recordings have been assigned by Dr. Bluemel to the American Speech and Hearing Foundation.

To quote Dr. Bluemel: "In the broad medical concept, the riddle of stammering involves a good deal more than speech. It involves the stammerer's personality, his native non-fluency, his environmental stresses, his disorganization in the sphere of speech, his struggle with the speech block, his conditioning experiences, and the final phase of phobia. Manifestly, the treatment of stammering requires something more than 'speech correction.' It calls for a broad psychological approach."

In the chapter on "Principles of Therapy" there are six diagrams which illustrate the process of speech learning and its progressive disruption in non-organized speech and in the various phases of disorganized speech; that is, in stuttering, in primary stammering, and in secondary stammering. Therapy is directed to the verbal thinking process. The child is helped through speech games which afford sensory—ear—training; and much effective speech therapy can be conducted in the home.

The adolescent and adult work consciously with their *inner* speech, endeavoring to establish a pattern of fluent verbal thinking. If the stutterer can learn to think quietly and clearly in words, he can "broadcast" the words to his mouth since talking is merely

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the process of thinking out loud. The techniques are described in detail.

The chapters entitled "The Speaker Himself" and "Retrospect" are rich in encouragement.—*R. M-S.*

Citation for Advertising Series

The American Medical Association, at its meeting in New York last month, awarded a citation to Parke, Davis and Company for "service performed to the public and to the nation through a continuing series of institutional messages published in national magazines, which accurately and dramatically tell the story of medicine and medical progress. . . . Because of these outstanding contributions to the public understanding of medicine, you have proved yourself deserving of this special recognition."

The pharmaceutical company began advertising in national magazines on behalf of the medical profession in 1928, and since that time has published 246 advertisements, most of which have dealt with socio-economic and health education topics.

This year the *Saturday Review's* advertising survey gave Parke-Davis a citation for its public service campaign in 1956, primarily dedicated to explaining the cost of medical care. The company has consulted with representatives of the American Medical Association frequently over the years in order to present advertisements which would encourage people to make full and wise use of medical services in the United States.

Committee to Combat Influenza

An advisory committee of physicians to consider precautionary steps in the United States against the current influenza epidemic in the Far East has been appointed by Dr. Leroy E. Burney, surgeon general of the Public Health Service.

The epidemics in the Far East have been caused by a new strain of influenza virus which apparently is not controlled by current influenza vaccine. It has been relatively mild, marked by a three- or four-day period of fever and other typical flu symptoms.

The Public Health Service has provided samples of the new influenza virus to manufacturers of vaccine in this country. Consultations with manufacturers will be continued during coming weeks on the possibilities of producing vaccine for general distribution if this should be indicated.

Travelers from the Orient and the Philippines are advised to see private physicians if they develop a respiratory illness within 10 days after their arrival in this country. The names and addresses of passengers having respiratory illnesses when they arrive will be forwarded to health officers in the communities to which they are going.

Surgical Federations Formed

The formation of federations of surgeons on a continental basis under the aegis of the International College of Surgeons was announced recently by Dr. Max Thorek, Chicago, founder of the college. The need for such organizations developed, he said, as a result of the rapid growth of the international college since its founding in 1935 in Geneva.

Four units have been established, covering North America, Central and South America, Europe, and Asia. National sections in 40 countries will form the nuclei of the federations. Dr. Curtice Rosser of Dallas, president of the United States section and professor and head of the department of proctology, Southwestern Medical College, will be the regional secretary of the North American Federation.

The international college has sections in all of the principal countries of the world with the exception of Russia and its satellites.

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Allergic disorders of infants include gastrointestinal disturbances, infantile eczema, urticaria and asthma. Gastrointestinal allergy may be manifested by vomiting, colicky abdominal pain and diarrhea. Allergic dermatitis may be evidenced by wheal-like cutaneous reactions which may develop into exudative lesions over the scalp, face and body. A systemic food hypersensitivity may produce an asthmatic response manifested by dyspnea and wheezing, although infection is usually associated with this type of response.

Common treatments include avoidance of the allergen, desensitization, antihistaminics and, in the presence of infection, antibiotics. Infants sensitive to the proteins of cow's milk whey may be fed human, goat or mare's milk reinforced with KARO® Syrup. Casein-sensitive infants may be offered soybean milk or amino acid mixtures reinforced with KARO Syrup.

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1	12	13	2½	4	6	390
2	15	13	3	4½	6	480
3	17	9	3	5	5	520
4	20	11	3½	6	5	610
5	23	11	4	6½	5	700
6	26	10	4	7	5	760
7	28	11	3	7½	5	740
8	30	11	2½	8	5	750
10	32	9	2	8	5	760

EVAPORATED GOAT'S MILK FORMULAS

Age Months	Weight Lbs.	Evap. Goat's Milk Oz.	Water Oz.	KARO Tbsp.	Each Feeding Oz.	No. of Feedings in 24 Hrs.	Total Calories
Birth	7	6	12	1	3	6	290
1	8	8	16	2	4	6	395
2	10	9	14	3	4½	5	520
3	12	10	15	3½	5	5	590
4	14	12	18	4	6	5	695
5	16	12	21	4	6½	5	695
6	17	13	22	4	7	5	730
7	18	14	21	3	7	5	710
8	19	15	20	2	7	5	690
10	21	16	16	1	8	4	730

LIQUID SOY MILK FORMULAS

Age Months	Evap. Milk Fluid Oz.	Water Oz.	KARO Tbsp.	Each Feeding Oz.	No. of Feedings in 24 Hrs.	Total Calories
Birth	6	12	2	3	6	380
1	8	16	3	4	6	532
2	9	14	3	4½	5	576
3	10	15	3½	5	4	650
4	12	18	4	6	5	768
5	12	21	4	6½	5	768
6	13	22	4	7	5	768
7	14	21	3	7	5	796
8	15	20	2	7	5	780
10	16	16	1	8	4	764

DRIED SOY MILK FORMULAS

Age Months	Dry Milk	Water Oz.	KARO Tbsp.	Each Feeding Oz.	No. of Feedings in 24 Hrs.	Total Calories
Birth	6	20	2	3	7	360
1	8	22	2	4	6	440
2	9	24	2½	4	6	510
3	10	29	3	6	5	580
4	12	33	3½	7	5	690
5	13	33	3½	7	5	730
6	14	33	3½	7	5	740
7	14	33	2½	7	5	710
8	15	33	2	7	5	720
10	15	33	2	8	4	720

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ABSTRACTS FROM CURRENT LITERATURE

Vascular Hemophilia

Schulman, Irving, et al.: Vascular hemophilia—a familial disease, hemorrhagic in males and females characterized by combined antihemophilic globulin deficiency and vascular abnormality, Pediatrics 18:3, 347-361 (Sept.) 1956.

A vascular basis for this disease was suggested in 1941 by McFarlane, who described morphologic and functional abnormalities of the capillaries of the nail beds in five cases. The capillaries were tortuous, distorted, and failed to constrict normally on trauma. Recently defects in prothrombin consumption have been demonstrated along with the vascular defects.

The authors present a study of four boys and three girls with vascular hemophilia. All had hemorrhagic tendency since infancy. One had an intracranial hemorrhage at birth with a slight hemiparesis. The most common bleeding manifestation in the other six children was severe and spontaneous epistaxis, requiring nasal packing and transfusions. There was excessive hemorrhage from the gums following loss of deciduous teeth or dental extractions. A history of bleeding tendency in the parents was positive in only two instances. Platelet counts, platelet morphology, prothrombin time, clot retraction, and concentrations of fibrinogen in the plasma were repeatedly and consistently normal in the seven children. The bleeding time (Duke) was prolonged in all seven. In four it was over 15 minutes and in the others it was 6 to 10 minutes. It was found that the deficient coagulation factor was antihemophilic globulin, which was shown in two ways.

Administration of fresh plasma resulted in correction of both bleeding time and coagulation defects in a patient with the combined vascular-coagulation abnormality.

Thus there are two groups under the classification of von Willebrand's syndrome, patients with vascular defect plus AHG deficiency (vascular hemophilia), and patients with vascular defect and normal coagulation status (pseudo-hemophilia).—*D.R.D.*

Obturator Hernia

Harper, Jack R., and Holt, James H.: Obturator hernia, Am. Jnl. Surg. 92:4, 562 (Oct.) 1956.

Obturator hernia is not common, although it is often mentioned in the differential diagnosis of symptoms referred to the lower abdomen, pelvis, and upper thigh.

The obturator foramen is nearly occluded by a dense membrane from the respective surfaces of which arise the internal and external obturator muscles. Through an opening in its upper forward aspect course the obturator vessels and nerves. The space (about 1 cm. in diameter) around these structures is normally closed by a pad of fat. When, because of emaciation or other factors, this fat is deficient or displaced, a canal is opened into which the overlying peritoneum may bulge. The female pelvis, especially in the multipara, is more prone to hernia in this area than is the male. The sac tends to lie anteromedial to the nerve and vessels.

These hernias occur mostly in women over the age of 60 years. Because of the small, hard, unyielding ring, these hernias are apt to strangulate, usually involving the small bowel, partially (Richter's type) or completely.

Diagnosis is aided by the Howship-Romberg sign. This consists of pain or paresthesia over the skin of the inner lower two-thirds of the thigh. Extension, adduction, and internal rotation of the thigh increase the pain of the hernia. In some cases a mass may be felt on the anterior pelvic wall, at the point of egress from within, by vaginal or rectal examination. This mass lies below the iliac vessels and the brim of the true pelvis.

Treatment is surgical by way of a pelvic laparot-

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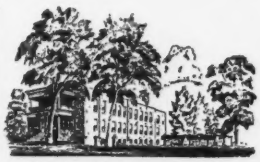

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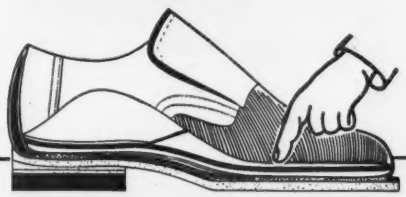

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omy. In order to release the hernia, it may be necessary to cut the obturator membrane in anterior-medial direction just below its insertion into the under surface of the superior ramus of the pubis. Some form of closure of the defect on its inner surface is effected, and the bowel dealt with according to its viability. An approach through the thigh is considered inadvisable because of limited access to the hernia and no access to the bowel after reduction.

The authors add two cases to those previously reported, bringing the total to 463, as of July, 1955. Resection of a gangrenous loop of ileum was necessary in one of their cases. Both recovered.—*T.P.B.*

ANNOUNCEMENTS

International Conference of Ultrasonics in Medicine, sponsored by American Institute of Ultrasonics in Medicine, Statler Hotel, Los Angeles, September 6-7. Write the Secretary, Dr. John H. Aldes, 4833 Fountain Avenue, Los Angeles 29, California.

Seventh congress of Pan-Pacific Surgical Association, Honolulu, Hawaii, November 14-22. All physicians invited. Write the secretary, Dr. F. J. Pinkerton, Room 230, Young Building, Honolulu, Hawaii.

Annual award of $1,000 (first prize $500, second prize $300 and third prize $200) offered by American Urological Association for essays on results of clinical or laboratory research in urology. Closing date December 1. Write the secretary, Dr. William P. Didusch, 1120 North Charles Street, Baltimore, Maryland.

Prize of $350 offered by Caleb Fiske Fund of Rhode Island Medical Society for essay on "Hormonal Relationships in Breast and Prostatic Cancer—Their Practical Application." Closing date December 31. Write the secretary, 106 Francis Street, Providence 3, Rhode Island.

The American people spent more than $11.8 billion for personal health services during 1956, Health Information Foundation reports. More than 25 per cent of this sum, or almost $3 billion, was covered by voluntary health insurance.

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Index to Advertisers

American Meat Institute 487
Ames Company, Inc. ..... Inside back cover
Ayerst Laboratories ..... XVI and 502

Bayer Company XI
Burroughs Wellcome and Company X

California State Personnel Board 496
Central Aircraft Charter Service 501
Ciba Pharmaceutical Products, Inc. 495
Corn Products Refining Company 497

Estes and Company, Inc. XIV

Fairmount Sanitarium 499
Foot-so-Port Shoe Company 499

Geigy Pharmaceuticals 491
Goetze Niemer Company 496

Hanicke, P. W., Manufacturing Company XVIII

Kansas Oxygen, Inc. XVIII

Lakeside Laboratories V
Lattimore-Fink Laboratories 499
Lederle Laboratories ..... VII, VIII, IX, XV, 489, 558, 559, and facing VI
Lilly, Eli and Company XX

Medical Protective Company 500
Menninger Foundation 499
Munns Medical Supply Company, Inc. 500

Neurological Hospital 498

Parke, Davis and Company ..... Inside front cover and III
Petro's Surgical Appliances 498
Pfizer Laboratories XIII
Physicians Casualty Association XVIII
Prairie View Hospital 502

Riker Laboratories 485
Robins, A. H., Company, Inc. 493
Roerig, J. B., and Company XVII

Schering Corporation ..... XIX and facing XII
Searle, G. D., and Company ..... XVI and 483
Smith, Kline and French Laboratories ..... Back cover
Southwest Scientific Corporation 499
Squibb, E. R., and Sons VI

Wallace Laboratories, Division of Carter Products, Inc. ..... Facing 492
Winthrop Laboratories, Inc. XII

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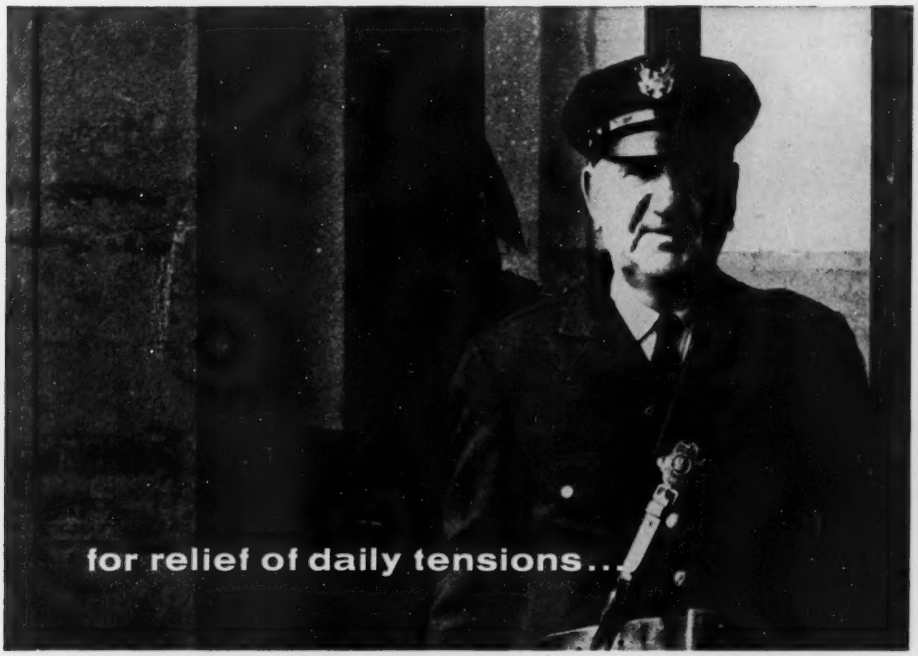

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*Ferguson, J. T., and Linn, F. V. Z.: Antibiotic Med. & Clin. Therapy *3*:329, 1956.

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1. Cornbleet, T., and Barsky, S.: The Role of the Tranquilizing Drugs in Dermatology, presented at 115th Annual Meeting of Illinois State Medical Society, May 19, 1955.

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

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